SCIENCE

VOL. 101 — FRIDAY, MAY 11, 1945 — No. 2628

SCIENCE: A Weekly Journal, since 1900 the official organ of the American Association for the Advancement of Science. Published by the American Association for the Advancement of Science every Friday at Lancaster, Pennsylvania.

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Annual subscription, $6.00 — Single copies, 15 cents

DISEASE OF THE HEART[1]

By Dr. ALFRED E. COHN

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As natural scientists we ought, I think, to seek earnestly and intelligently the place where our science fits in the general scheme of knowledge. Because there has been some measure of carelessness, the need is greater now, when exact methods of thinking are beginning to be used in the study of diseases. So much is usually included in accounts of disease in general, and of any set of diseases in particular, that what constitutes the essential properties in the description of any disease and so of diseases in general is often obscure. These remarks apply with especial relevance to disease of the heart. Folklore, tradition, anatomy, early physiology, contributions of the art of the clinic, bacteriology and therapeutics have all been included indiscriminately in accounts of the history of knowledge of this organ. How much earlier than Aristotle attention was paid to the heart and circulation is of little importance. The heart was recognized in any event as an organ of very great significance. Aristotle recognized in its performance the existence of rhythm. And rhythm in nature has been a subject which has always compelled speculation—whether this is applied to the daily reappearance of light or whether to the tides in the Euripus, in the case of Aristotle. Mention of Aristotle has value because it indicates when records on this subject began. It was not until about two thousand years later, in the middle of the eighteenth century and the early decades of the nineteenth, that a sensible contribution was made by any one to a recognition, to say nothing of an understanding, of the

[1] Delivered before Alpha Omega Alpha, Tulane University Medical School, New Orleans, March 20, 1945.

existence of any disease of the heart. I pass over the names of Galen and Erasistratus, of Leonardo and Vesalius, of Servetus and Harvey. Whatever contributions to knowledge they made, and many of them were not only striking but of determining importance in anatomy or in physiology, I pass them without further mention because these advances were not additions to a comprehension of the evolution of knowledge concerning disease or diseases. Morgagni, Pitcairn, Wells, Corvisart, Laennec and Hope occupy wholly different positions.

But before I discuss observations, I should define what disease may mean and I should make an effort to discover why a society like ours is concerned with this problem. I have mentioned the word "science." It is by no means clear what subjects are to be included in this term. Investigations on light and magnetism and matter, both inorganic and living, have earned them the right to belong here. They are present everywhere. The most critical thinking and the most rigorous methods of which we are capable have been applied to them. These phenomena have universality. The universe is not to be understood unless they are. They are essence—not accident. But diseases—do they partake of this nature? And if they do not, what special considerations apply to them to separate them off? The answer, I think, is simple. Diseases are not timeless nor are they found everywhere. Some of them have appeared for brief periods only—others are confined to limited localities. Many are accordingly not necessary. Whether certain other ailments are to be designated diseases is not clear but not unimportant either; they appear not separable from the life and growth of the human organism. Some which are accidental are, just now, during wars carried on everywhere on the planet, introduced upon these shores for the first time, brought here by returning soldiers, illnesses never encountered in this country before.

It is desirable to widen this inquiry and to study where diseases are endemic and under what conditions they spread from their original to other regions. Diseases are, in short, linked both to space and time. These characteristics make them different from natural phenomena which have not these limitations but which have continuous and enduring existence. By contrast it makes of diseases something which gives them the appearance of accident. I believe that these elements of difference have far-reaching consequences for the advancement of knowledge, for the education of those who wish to advance that knowledge and for the place of diseases in our scheme of things—social, intellectual and economic.

How long, do you think, will diseases like typhoid fever or malaria continue to be studied when these diseases cease to afflict human beings? Compare the number of publications on the subject of typhoid fever in the year 1900 with those in the year 1943, in the midst of a great war. Or take the case of malaria. How long will the many problems connected with mosquitoes as vectors or matters connected with the human carriers of this disease or the symptoms that occur in its many forms or the chemotherapeutic investigations now being conducted so energetically survive, after the dusting powder DDT has rid us of the insects which convey this ubiquitous and destructive disease? I wish naturally not to be misunderstood. There is good ground for believing that gifted and curious men will continue to interest themselves in the biology of pneumococci, in the processes of immunity, in the life cycles of plasmodium malariae. These are general problems of enduring interest, come to notice because once they were injurious. Interest in them may survive because they yield occasions for gaining insight into processes of living—a better occasion than when they did so into processes of killing.

In considering disease of the heart these wider generalizations can be applied. It is certain already that this organ is liable to diseases which belong in the category of accident; but the heart gives rise also to ailments in other categories, the meaning, and therefore the classification, of which is far from established. A first rough approach to ascertaining the significance and importance of cardiac ailments can be gained from engaging in so colorless a business as trying to learn the number of persons in this country who are incapacitated by cardiac disabilities—what kinds of persons do they afflict; do they afflict all the victims at every or only at certain ages; and do they do so everywhere or in selected areas only? Answers to these questions will themselves, if given consistently year after year, introduce concreteness and definition into our inquiry, and put us on the road to appreciating more than one fact of great significance. I have inserted the phrase "year after year" not without purpose. We live always in states of transition; nor have the past hundred years escaped this quality. But the last forty suffice to bring into prominence one aspect of change—especially important in this study. In this period the outstanding elements that demonstrate that this is a period of transition can be made evident from an analysis of the population and its illnesses—treated statistically. In the transition, forces have been at work which have modified the composition of our entire population and have brought in their train a variety of consequences in the economic life of the country, the end of which is not yet in sight and a comprehension of which has just begun to engage the national interest.

On what factors have the changes depended? In an era, the beginning of which is arbitrarily chosen at

the year 1900, deaths from infectious diseases such as typhoid fever, tuberculosis, intestinal infections, both in infancy but also at more advanced ages, were rampant and, through death, permitted relatively few people to attain old age. These diseases now have all but disappeared. There is room here for misunderstanding that should by all means be avoided. These diseases still exist. The numbers affected are great. The suffering which is entailed in individuals is not less than it was. But the grand total of persons who are involved in such misfortunes has shrunk to a much lower level. The direct consequence of the significant reduction of diseases which took their great toll of persons in the first two or three decades of life has resulted, naturally, in the survival of those same persons into the sixth, the seventh and the eighth decades. When we say, therefore, that expectancy at birth has increased greatly, emphasis should be placed at the same time on the fact that the phrase—expectation at birth—does not include as a consequence increase in the number of years it is possible to live. It means only that more persons are in position to realize a span of years which, within the range of those variations observable among men, make possible the attainment of natural expectations.

Now, what has been said permits insights into the state of affairs as to diseases of the heart. The names which are given to diseases have very great importance. If as descriptions they are inadequate or inaccurate, their use can be seriously misleading in laying out conceptions of the health of the nation. It is a comfort to realize that the business of using correct nomenclature is now taken seriously and that improvement is demanded. That increases confidence in statistical enumerations. There need be little doubt, therefore, in accepting the statement that certain names, that is diseases, occur with decreasing frequency in the earlier decades. Other ones occur with increasing frequency in the later decades. It is also a fact that during these last forty years, fewer and fewer entries are to be found before the age of forty. Young people, in short, are dying less and less of any cause, certainly of infection. Many, many more older persons, on the other hand, appear in the mortality tables. Of what are they dying—of the same diseases as the young or of other ones? And if of other ones, are those peculiarly appropriate to their age? That is a crucial question, bound up in the phrase "peculiarly appropriate." In the end, we shall agree there is a difference between the processes which cause death among the young and those which do so among the aged. Concerning those which result in death among the aged, knowledge is far from precise. If they are different there is still opportunity for difference in opinion concerning their nature. About their occurrence there can be no doubt. They have forced themselves upon our notice.

The whole circulatory system exhibits seemingly natural, evolving processes—in the heart, the arteries, the capillaries, the veins and those parallel and accessory systems which see to the movement of fluids through the body. All these several parts are subject to injuries which create in them something unusual and are therefore abnormal or diseased. The most significant factor in bringing about change in performance or function is often not definitely known even when its nature is suspected, as is now the case in many directions. With this general reservation it is possible to proceed as if what is now known constituted genuine insight into malfunction. It is appropriate to speak of the heart first. It is not as if the heart were composed of a single tissue. The several of which it is composed each requires consideration of its own account. Its bulk consists predominantly of muscle, a fact never to be forgotten. The arrangement of that muscle is far from simple. It is in fact a system of intricate bands which form figures of eight in three dimensions, a very powerful mechanism. The muscle fibers which compose it differ in structure from all other muscle cells in the body, smooth or striated. The life of this mass of muscle depends upon its blood supply—conveyed to it by an elaborate system of coronary vessels. The rich supply of nerves and ganglia play an important role in the behavior of these muscles, whether by dominating its performance or instead of regulating the harmony of that performance, is still not wholly decided. Of another structure which presides over the sequential coordination of the auricles and ventricles there need be no mention now.

But it is important to move into a position of great prominence the endothelial layers which cover both the outer and inner surfaces of the heart, and of that surpassingly ingenious arrangement of valves within, which for several reasons have occupied so large a part of the attention and which eluded so successfully for so many centuries the imagination of men in picturing forth the mechanics of the heart's action. However the whole story may ultimately be written, and in whatever way and on whatever ground they come to be involved, the inflammations of the valves, together with that of the endothelial lining of the heart, constitute processes in this organ which are to be found almost exclusively in younger persons—the infectious diseases predominantly but not exclusively of the endocardium of the heart.

In young people, rheumatic fever is the disease which stands at the head, indeed far in the lead, of all the diseases of the heart. It is, at that age, the out-

standing disease of the endocardium. All the anatomical features of this disease are not yet known, and although there are theories aplenty concerning the bacterium or bacteria which occasion this disease, and concerning the other very intricate immunological principles which are at work, definitive knowledge on its etiology, although it does not exist, seems, will-o-the-wisp-like, to be beckoning just around the corner. Presumably there are weaknesses or local chemical attractions in the endocardium, or defects in the structure of the valves, a point on which Thomas Lewis has laid stress, that dispose these structures to invasion by bacterial and perhaps virus diseases.

Now the course of events, after rheumatic fever has been acquired, is various and unpredictable. A first attack may last a brief time only, but be overwhelmingly severe, so that a patient dies in the first one, in a matter of days. Or, even after having suffered a series of recurrences, not too severe perhaps, a patient may survive and may actually fill out his expected days. In any case a further account of this subject is not relevant here.

It is for the sake of completeness worth recording two other diseases which belong in this class and affect younger persons predominantly even if not exclusively. These are cardiovascular syphilis and bacterial invasions by streptococci, pneumococci and rarely, gonococci.

These then are the ecological, the environmental, diseases. They are of two classes; first those in which the host is an opportunity for parasites, mostly living—the bacteria. Second, in very recent years, since the dividing line between living and non-living things has become much more sharply drawn, structure alone being decisive in determining the existence of livingness, quasi-living things also may play a role. Such entities, viruses, can, it is now certain, take on the function of being agents inciting disease. This conception is the consequence of Stanley's discoveries beginning with the virus of tobacco mosaic. All this concerns the milieu exterieur, though the problem of susceptibility, the corresponding reaction of the milieu interieur, may naturally not be ignored.

The dependencies on time and place give to the study of ecological diseases a peculiar accidental appearance, different from the universal nature which characterizes the steady march of inherent ailments. Concerning ecological diseases we do what we must—not what scientific curiosity dictates. All the so-called infectious, communicable, contagious diseases belong in the ecological group. Since they vary with time and place, that is to say with climate or geography, it has been customary, and indeed imperative, to study only those diseases which threaten or actually disturb or endanger us. It is a matter of common sense, therefore, that we devote ourselves only to those which are upon us.

When they exhibit wide-flung biological principles which reward exacting study, the situation is different and we change our attitude.

In addition there are diseases which depend not on the milieu exterieur but on the behavior of the whole organism as an expression of harmonious existence. They depend, I am suggesting, upon the milieu interieur. It requires only a cursory glance at a graphic record of mortality to notice that the number of persons who succumb to attacks of infectious diseases in early years is, relatively speaking, insignificant in comparison with the great number of individuals, now to be discussed, who die in ever expanding numbers after age forty-four. It is almost as if, having survived the struggle of the first year of life and having established one's right to live, the chances are very good that you can go on until old age, and good perhaps even to advanced old age. This statement is almost correct. It needs, however, a few modifications. One is important enough to be singled out to the neglect of the others. The record shows that there is one cause of death which begins to take its toll already in the fourth and fifth decades, that it increases in destructiveness decade by decade until it becomes dominant, and in the end overwhelming. Here is an arresting observation; it may yield information of importance.

Because cardiac deaths begin so early in life it seems unlikely that those which take place in the fourth and fifth decades are identical with those which occur later—in the sixth, seventh and eighth. Supporting evidence that they are different begins to emerge. The whole story needs still to be unfolded. If there were no ecological or accidental reason for dying in the earlier decades, there may be, and in all probability are, other reasons connected either with one's inheritance or with some other form of subtle injury, exposure to which has long been going on, but has not been recognized.

In this milieu, the milieu interieur, at least two different kinds of process are distinguishable—hormonal ones which for some reason, often not identified, disturb the balanced life of the body and result in disharmony and so, in disease. But much more important, indeed overwhelmingly important, in these interior disturbances are the ones which are recognizable as the ailments and disabilities of the aging process. These phenomena are, it seems, intimately associated with the evolution of the body and may be called disturbances inherent in its natural history.

It is necessary to call attention, in passing, to differences in the liability of diverse races to suffer

n ailments or disabilities peculiar to themselves that these are occasions for assembling informa- concerning duplicate natural histories. They d not be described in detail here.

n this background, free choice can and should be rcised in deciding what researches come first. In king a selection the quality which we call states- nship becomes determining. And the technique ich statesmen employ turns out to be statistics. t technique applied to phenomena expressive of condition of the public health gives the clue to t it is urgent to investigate. "In early use (A.D. 7) (statistics was) that branch of political science ling with the collection, classification, and discus- of facts . . . bearing on the condition of a state community." (O.E.D.) That early use of the d statistics deserves to be reintroduced, at least common comprehension.

t is desirable now, to be definite. The heart is a ge organ. Its weight depends, except for a few cent., on its muscle. The fate of the muscle is be taken with great seriousness. But it is unlikely t the muscle lives unto itself alone. Its arrange- nt is complicated, the fibers branching in all direc- ns, so forming a syncytium. The coronary system vessels is so arranged as to supply at least one pillary to every fiber. The number of muscle fibers obably does not change from birth to death. But intimate structure of the fibers alters considerably. ughly, very roughly, a fiber at the beginning of e appears not to contain very much aside from its cleus, not much even in the way of sharply defined ss striations. But later on, certainly at middle e, a fiber seems to contain a good deal. Beside a cleus, cross striation is conspicuous and curious uctures called cement lines, intercalated discs, step- e concentrations like boundaries, make their ap- arance. The nucleus itself, instead of looking a ple featureless ovoid globule, begins to look like angry cumulus cloud. In youth cross striations e everywhere evident, running like bars to the very ge of a nucleus. But later, outside both nuclear les there are spaces, become vacant of striations d now filled with lipochrome pigment. The meaning all these changes from youth to age is not obvious. t one thing may be taken for granted: there is an escapable relation between the form of a structure d its function. What that relation is, is far from ving been worked out. Here enter two important oblems. One concerns the nutrition of the muscle; d the second, its essential function, its motion, the siness of contraction. One question which needs be asked of the muscle fiber is this—is the altera- on in its form connected with its nutrition? If, her things being equal, and the other things are difficult even to define—if the composition of the blood remains uniform throughout life, would any change in the form of the muscle take place? In one sense this is an idle question because it is already known that the organs of the body do not develop synchronously. Evidence for that is to be seen in the decrease in size of the thymus gland in childhood and in continuous changes in the structure and function of the genital tract both in males and females. Whenever an organ or a tissue changes, there must go with that a discharge into the blood stream of modified and perhaps of new substances, each of which plays its role. Clearly with changes such as these, whether cyclical or otherwise, reflections of these changes must and do occur in the blood. What is obvious in these examples has counterparts in the behavior of many or all the other organs and tissues of the body, each after his kind.

The blood, which is our common supply and disposal system, accordingly changes. What else changes? How the endothelial reticulum lining the capillaries does and how the other elements in their walls, lying between the blood stream and the muscle fibers, is not known with particularity. But there begins to accumulate evidence to show that this is so. There are, it seems, then, changes of three kinds; in the blood, in the capillary wall and in the muscle. All change, but to what end no one knows.

There need be no question about the labor of the heart; that is carried on by its muscle. What concerns or damages the muscle, other things like the valves being equal and uninjured, concerns a man's strength and indeed concerns his very life. What function limits the power for work so that after thirty-four or thirty-five a man is not as fit an instrument for military service as he was formerly? That same function is the limiting factor also in his athletic performance and in the expression of his vigor in general. It is not necessary to believe that the lessening of physical power is dependent solely upon the muscle of one's heart. Undoubtedly, owing to the togetherness of the whole organism, all his structures participate in his performance. But the muscle of the heart certainly participates as one of them.

The word contraction serves to denote that power of the cardiac muscle fiber on which the development of vigor depends. If that decreases what can there be in that increasingly intricate structure of a fiber which spells, as it were, the decline of its power. It is of course not necessary that the most significant contribution in a system should be that element of which there is most bulk. Nor is it obvious as yet which constituent of a muscle fiber plays the outstanding role in the act of contraction. The intricate arrangement of the lines of cross striation and the vary-

ing height of the discs between the recurring main ones suggest that they may not be ignored. But so far they have not been studied successfully, either chemically or otherwise, to this end. Such a study presents for the time being too great a challenge to current technological refinement. Instead, advantage has been taken, especially by Mirsky, of the opportunity to study, as such, the proteins that occur in muscle. It turns out that they constitute the most important bulk (19 per cent.). And of them, myosin is the protein which is present in largest amounts (two thirds). Reversibility of denaturation is now recognized to be an important function at least of certain proteins. This study, after having made progress for a while, has recently slowed down. That is unavoidable. Such episodes suggest an analogy with military operations, which teach that a salient can not safely be thrown forward indefinitely without collateral support. The shoulders must be consolidated. In the slow advancement of knowledge it is necessary to await from time to time for the study of neighboring subjects to come abreast. But sometimes you stop, even in mid-career, just short of success, for reasons not dictated by the experimental situation. Moses you remember did not enter the Promised Land.

In assigning reversibility as a property of a protein, myosin for example, underlying the act of contraction in a given structure and as responsible for that act, certain considerations must be satisfied. Among them it is necessary to know how many times a minute the action takes place. A number of years ago, in 1911, Hertz and Goodhart encountered a case in which the speed of the heart, that is of the ventricles, was recorded at 236. They thought the number 236 represented the speed limit. Later, rates as high as 313 have been found. What cardiac muscle can do is, of course, not limited to such observations. The bearing of fibrillation and flutter on this function is not yet obvious. But it is clear that if reversibility of denaturation of myosin or of any other protein determines the act of beating, the rate of reversibility which is possible in that protein is basic to a conception that the rate and rhythm of the heart depend on this substance.

That there exist muscles, change in the state of which can occur several hundred times a minute, is obvious in the speed of the wings of insects and of humming birds and in the hearts of canaries. Something accomplishes this trick and does so, obviously through the mechanism of a particular structure, situated undoubtedly in muscle. It seems almost inescapable that this something is basically protein, provided this has the faculty for accomplishing such continuous rapid changes. The responsible substance may, of course, wear away and so may need rapidly to be replenished. But it seems less likely that the result should be accomplished by using up a su stance, rather than that a substance should ex poised in unstable knifelike equilibrium to be set motion, from lengthening to shortening, by so master mechanism. Whether reversibility of d naturation is capable of such rapid oscillation is, course, still unknown. But if this is the directi in which search for the basic mechanism of rhythm contraction is to be instituted, some such process the reversibility of denaturation seems a possible co ception to explore.

There are good reasons for wanting to get on spee ily with advancing knowledge in this direction. contraction is essentially a chemical reaction, th here as everywhere, to be able to control such a r action, a knowledge of the chemical mechanism whi constitutes that reaction is essential. And if, furth more, the means at hand to establish control are i adequate, an attempt to alter a detail in the structu of a controlling agent and so to bring about a usef result is eminently desirable. These have been th considerations which underlie the plan of investig tion that has been going on in exploring the chemist of the immune processes and in the pharmacologi studies which are devoted to furthering those obje tives. And so, the disinterested (chemical) study the mechanism of contraction leads on to furth analyses having a practical value in therapeuti But there is even a further reason for this investig tion. Understanding the behavior of the substanc which engage in the act of contraction has theoret cally, and for many people preeminently, the gre advantage that it may facilitate not only comprehe sion of an important subject but may actually assi in illuminating that most subtle process, among th many subtle ones in nature, called growth, which i a special sense is the same as the process of agin The structure of muscle and its functions and th changes both in structure and function which tak place with time have, therefore, decisive importan in securing a better comprehension of the ailment of the heart at all ages, but especially those at th far end of life.

Turn now to the coronary vessels. They themselve aside from their function of being channels for ca rying blood and so of facilitating the nutrition o the muscle, have life histories of their own. Th newly identified disease, of which the observation of James Herrick have made us aware, is intimatel dependent on occurrences in the walls of these vessel That these vessels, especially the arteries, are subje both to microscopical and then to gross alteration beginning almost at birth, metabolically in the form of cholesterin deposits and structurally in splitting of the internal elastic lamina, has long been know Having begun with the discovery of changes in th

ic tissue, designated arteriosclerosis, and having ed of the subsequent introduction of fat and um in the ground substance, designated athero-osis, investigation has proceeded further. It has been learned which vessels in the coronary sys- suffer earlier from these processes, which ves- represent major importance from the point of of site, and what the consequences are to given s of muscle to which the vessels large or small distributed when these same vessels become im-able. Whether passage is interrupted gradually uddenly has, of course, clinical bearing. It is too much to say that knowledge of the proc-s to which the coronary vessels are subject and ultimate damage to which they give rise can be too minute. The fate of the very smallest seemingly insignificant capillary constitutes an ortant part in the mechanism of damage. But usion of a vessel, even of a capillary vessel, does tell the whole story. That is only the end of drama. Larval processes must have been going continuously in the walls of capillaries and of ries, perhaps in the vasa vasorum, which con-ute changes of such a nature as to alter their ucture and so to interfere with the passage of abolites. These processes injure the walls further, l so impair the nutrition of the muscle beyond. ground substance, where Aschoff thought the ic metabolic disturbances take place, deserves thermore the most thoroughgoing research. It is essary to think only of the capillaries in a glo-rulus of the kidneys or in an island of Langerhans in the convolution of Broca to appreciate the ent to which health depends upon the integrity l consequently upon the successful performance of se very small structures. So far, exact studies of larger arteries, but less of the smaller vessels in coronary system, have had rewarding results. ere is a difference, it is now known (Ehrich, de la apelle and Cohn) in the vulnerability, or perhaps would be better to say in the viability of various ronary arteries. The branch which supplies the ck of the heart (the posterior descending ramus) rvives intact, without lesions, for a decade longer than the one which courses down the front. Besides, there are sites along both these vessels and along the trunks from which they originate, which seem especially exposed to deformity. Why these sites? And when in a man's life are they affected? Is there a difference between men and women in the development of particular kinds of lesions? Blumgart, Schlesinger and Davis have carried on the search further and have shown that it is not only vessels at different locations but societies of vessels in several, perhaps special regions which under certain circumstances fall victims simultaneously to an underlying, far-reaching process.

These studies must go further. It is necessary to know what compromises the expectation of long duration in the competent life of vessels of different orders of size and in different locations and of whether a recognizable element exists, in metabolism perhaps, which accounts for what we observe. Is there a difference among the races of men, yellow, black and white, or in the conditions under which they live and nourish themselves, that brings about differences not only in the length of life they may reasonably anticipate but, to pass from the very important to the very minute, in the evolution, in the growth of their smallest blood vessels. These may be the differences, the growth and nutrition of their blood vessels, on which the health of their surviving years depends. We begin to appreciate the fact that on the mechanics of the infinitely small depends the mechanics of the great machine—electrons, valence, the very granules in cells, and genes in chromosomes, upon these depend the morals and intelligence of individual citizens in the highest and in the humblest places. To learn about such matters is not to go too far afield if we are to gain badly needed insights. What takes place in our later decades and what hope we may entertain in developing ability to manage the course of our lives may depend, not improbably, on our managing to live so that pain and disability is reduced and that we approach our appointed ends with a maximum of joy in living and with a minimum of dependence and decrepitude.

(*To be concluded*)

OBITUARY

A. D. E. ELMER

FROM a friend recently released from the Santo omas prison camp in Manila word has been received the death in July, 1942, of A. D. E. Elmer, the dis-nguished Philippine botanist. Working under great ndicaps, Mr. Elmer published ten volumes of Leaf-ts of Philippine Botany, and distributed sets of hilippine and Bornean plants to all the principal herbaria of Europe and America. Mr. Elmer was a plant collector of extraordinary ability. He graduated from the State College at Pullman, Washington, in 1899, and received a master's degree from Stanford University in 1904, leaving shortly after for Manila, where he made his home until his death. It was my privilege to know Mr. Elmer for over forty years. To hear him tell in his quiet way of fantastic but

perfectly true adventures and experiences during his early years in the Philippines, among wild people in remote localities, was a thrilling revelation.

ALBERT W. C. T. HERRE

RECENT DEATHS

DR. CARLTON C. CURTIS, who retired in 1934 as professor of botany at Columbia University, died on April 12. He was eighty years old.

PROFESSOR RAY KEESLAR IMMEL, dean of the sc of speech at the University of Southern Califo died on April 14 at the age of sixty years.

DR. FRANK R. ELDRED, consulting chemical e neer, died on April 15 at the age of seventy yea

DR. MARTIN HENRY DAWSON, associate profess clinical medicine at Columbia University, died April 27 at the age of forty-eight years.

SCIENTIFIC EVENTS

THE IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY

PLANS are being made for the celebration of the Centenary of the Imperial College of Science and Technology, Kensington. These, however, must be dependent on the progress of the war. An article on the history and plans of the college appears in *The Times,* London. It calls attention to the fact that the college, like many English institutions, came to being not by an act of new creation but by a fusion and development of earlier foundations. It is a federation of three constituent colleges—the Royal College of Science, the Royal School of Mines and the City and Guilds College (formerly the Central Technical College of the City and Guilds of London Institute); and these in turn were related to earlier institutions. The earliest of all was the Royal College of Chemistry, the foundation-stone of which was laid by the Prince Consort in June, 1846.

The Times writes:

By a Royal Charter of Incorporation dated July 8, all three were federated in one great college, unique in our educational system. (In the case of the City and Guilds College revised conditions of incorporation were approved by his Majesty in Council on July 19, 1910.) The Imperial College is an institution expressly charged with the provision of ''the highest specialized instruction . . . and the most advanced training and research in various branches of science, especially in its application to industry.'' Equally with pure science, technology is its primary concern; yet, alone at present among colleges concerned with technology, it devotes all its energies to work at university level. It is a ''peak institution'' comparable with the Massachusetts Institute of Technology, and the ''alliance'' concluded with that institution in 1944 was a recognition of community of aims and interests. Its Charter established it ''as a School of the University of London.'' Its visitor is his Majesty the King.

The need is urgent for new laboratories, new equipment and additional staff and income with which to extend the provision of "the most advanced training and research." But for these, it is pointed out, the college must look, as formerly, to public funds, and the people's need for houses must delay its buil program. Meanwhile in the college as it exists t is much that can be done, though under difficul to improve its amenities and to extend its corpo life.

CONFERENCE ON RESEARCH AND REGIONAL WELFARE

A "Conference on Research and Regional W fare" was held at the University of North Caro on May 9, 11 and 12. President Wilson Compton, Washington State College, gave the opening add with the title, "The Power of Ideas."

The Thursday morning session was devoted to general topic "Research in the South." Presid Raymond R. Paty, of the University of Alabu spoke on "The Development of Southern Researc and Dr. Wilbur A. Lazier, director of the South Research Institute, on "Research for Prosperity the Industrial South." In the afternoon papers w read by Dr. Russell M. Wilder, head of the D partment of Medicine of the Mayo Foundation, "Research in Nutrition: Importance to the Pu Health"; and by Brigadier General James S. Si mons, chief of the Preventive Medicine Service, Of of the Surgeon General, U. S. A., on "The Foun tion for Future Progress in Health and Public S vice in the South." The evening session was devo to research in the humanities and social scienc Professor Avery Craven, of the University of C cago, spoke on "History and Social Reconstruction and Professor D. C. Allen, of the Department of En lish of the Johns Hopkins University, on "Resea in the Humanities."

In the morning session, May 11, Milton H. F consulting engineer of Birmingham, Ala., planned make an address on "Research and Industry as a F tor in Southern Development" and Reuben B. Robe son, executive vice-president of the Champion Pa and Fibre Company, on "Needs and Opportunities Research in Industry." The afternoon was devo to fisheries and agriculture, with Dr. Harden F. Ta lor, recently president of the Atlantic Coast Fisheri Company, speaking on "Fisheries Research in Sout

n Betterment," and George J. Wilds, president of e Pedigreed Seed Company, of Hartsville, S. C., on Research and the Southern Farmer."

At the final session addresses were scheduled to be ade by Dr. David E. Lilienthal, chairman of the ennessee Valley Authority, on "Southern Development and Regional Planning," and by Undersecretary f War Robert P. Patterson, formerly president of e Standard Oil Development Company, on "Research and Industrial Development."

HE DEPARTMENT OF TECHNOLOGY OF THE CARNEGIE LIBRARY OF PITTSBURGH

In the fall of 1944 the Pittsburgh Section of the merican Chemical Society initiated a campaign to aise funds in support of the department of technology of the Carnegie Library of Pittsburgh.

This department was the first of its kind in any ublic library and for some years was one the finest echnical libraries in the country. Its files of older cientific periodicals are remarkably complete. Even o-day, there are on the shelves a few foreign journals ot found elsewhere in America. Material in the epartment is for reference use only, but thousands f circulating books in pure and applied science may e borrowed from the lending department.

The catalogue system is a unique type of classified, nnotated index which does not exist in any other library. The department has had the services of one of the outstanding technology librarians of the country, E. H. McClelland, but has lacked funds during recent years to maintain its former excellence; it has been open to the public eighty-two hours per week but has had to curtail rather than expand its service.

The section has had for many years a standing Library Committee, formed some years ago under a former section chairman, Dr. J. O. Handy, during whose administration the sum of $2,600 was turned over to the department. The library was then and still is supported by city funds and has no endowment.

Last summer, Dr. Gilbert Thiessen, chairman of the Library Committee of the Pittsburgh Section, began some constructive work to obtain funds for the department of technology. He gained the enthusiastic support of Dr. W. A. Gruse, then chairman of the section. As a result, a Technology Library Fund Committee was appointed. It included a number of scientific men—many of them directors of local research laboratories.

The work started by Dr. Gruse was continued by Dr. H. K. Work, the present chairman of the section, when he assumed office in the early part of the year. The work of raising the money was handled by C. G. Fisher, chairman of the Fund Committee, who has long been chairman of the Finance Committee of the Pittsburgh Section.

The Technology Library Fund was inaugurated with a goal set at $50,000. The Pittsburgh Section of the American Chemical Society contributed $2,000 from its treasury. Through the efforts of Mr. Fisher and his committee, the total amount of the fund is now $66,195. Most of it has come from industries, some of which are more than a hundred miles from Pittsburgh. A contribution of $10,000 came from the Buhl Foundation and others came from individuals.

The fund is administered by a seven-member committee consisting of representatives of the Pittsburgh Section of the American Chemical Society, the Mellon Institute for Industrial Research, the Carnegie Institute of Technology, the University of Pittsburgh and the technology librarian of the Carnegie Library of Pittsburgh. The present members of the committee are:

Pittsburgh Section, American Chemical Society: *Chairman-elect*, Dr. R. N. Wenzel; *Chairman of the Library Committee*, Dr. Gilbert Thiessen; *Chairman of the Finance Committee*, C. G. Fisher.

The Mellon Institute: Dr. W. A. Hamor.

The Carnegie Institute of Technology: Dr. B. R. Teare, Jr.

This committee confers regarding purchases to be made with the fund which is not an endowment but is designed to supplement the funds regularly made available; the department already has placed subscriptions for many new technical journals, and is again buying technical literature in accordance with the needs of the district. Although the amount to be expended as initial outlay and for the maintenance of subscriptions each year will vary, it is estimated that the fund will be sufficient for several years.

The library fund will not be restricted to the purchase of chemical literature. Chemists are represented in all industries and utilize the technical developments of all branches of science. The fund is designed to enable the department to regain, and to improve upon, its former service in providing reference literature in the entire field of pure and applied science—the whole field of technology in its broadest interpretation.

THE FIFTIETH ANNIVERSARY OF THE NEW YORK BOTANICAL GARDEN

There has been formed a national committee of more than one hundred members, sponsors for the Fiftieth Anniversary Celebration of the New York Botanical Garden. John W. Davis, formerly ambassador to Great Britain, has accepted the chairmanship. The committee includes prominent botanists, scientists and industrial and lay leaders in all parts of the nation.

The fiftieth anniversary will be observed in various ways throughout the year. The first major event of

the observance will be Anniversary Garden Week, from May 14 to 20.

On Sunday, May 13, the garden will be rededicated in a special program in which Mayor LaGuardia, Commissioner of Parks Robert Moses and Bronx Borough President James J. Lyons will participate. Hosts at the rededication program will be Mr. Swan, Dr. Wm. J. Robbins, director of the garden, the garden staff, members of the Board of Managers and members of the Advisory Council. The garden, a private corporation, is financed by municipal appropriations and by gifts, memberships, bequests and private endowments.

At the conclusion of the brief speaking program, the official party will make a tour of the grounds, traveling in the trains which were operated at the New York World's Fair. These trains will be at the disposal of the general public during anniversary week.

A series of special days is being arranged for the anniversary week. The first of these to be announced is International Day, on Saturday, May 19. A special program will be presented, opening at 3 P.M. Greetings from the heads of many botanical gardens in foreign nations will be presented by Dr. Robbins. A series of nationality dances will then be presented, to be followed by general folk dancing. The dance programs will be under the direction of Mrs. Michael Herman of Flushing.

SCIENTIFIC NOTES AND NEWS

PRESENTATION of the second award of the Richard Pearson Strong Medal for outstanding service in the field of tropical medicine, and of an honorarium of $500, was made at a recent meeting of the American Foundation for Tropical Medicine to Rear Admiral Edward R. Stitt, former Surgeon General of the United States Navy, by Colonel Richard Pearson Strong, director of tropical medicine at the Army Medical School.

DR. GEORGE SANTAYANA has been awarded the Nicholas Murray Butler Gold Medal of Columbia University for his book "The Realm of Being," a treatise on metaphysics. The medal is given every five years for the most distinguished contribution anywhere in the world in the preceding five years to philosophical thought or to educational theory, practice or administration.

THE presentation of the Baekeland Medal will be made to Dr. Edwin R. Gilliland on May 14 at a meeting in Newark of the North Jersey Section of the American Chemical Society. On this occasion Dr. Gilliland will give an address on "The Synthetic Rubber Industry." Dr. Maximilian Toch will speak on "Baekeland, the Young Chemist," and Dr. W. K. Lewis on "Gilliland—an Estimation." The presentation will be made by George Baekeland. The award was made in recognition of outstanding achievement in the fields of heat transmission, diffusion, distillation and high pressure synthetic chemistry.

AT the meeting of the Board of Directors of the American Chemical Society in Washington on April 16, the Award in Pure Chemistry (sponsored by Alpha Chi Sigma) was conferred on Frederick T. Wall, of the University of Illinois; the Borden Company Award in the Chemistry of Milk was given to Ben H. Nicolet, of the U. S. Bureau of Dairy Industry, and the Eli Lilly and Company Award in Biological Chemistry to Max A. Lauffer, of the University of Pittsburgh.

AN oil portrait of Dr. Ludvig Hektoen, one of the founders of the Institute of Medicine of Chicago, for twenty-one years chairman of its Board of Governors and now honorary chairman, was presented to the institute as a gift from its fellows on the afternoon of April 25. A large number of the fellows and their wives were present at the reception to greet Dr. Hektoen and to pay tribute to his long record of distinguished service to the medical profession. The portrait, painted by Carl Tolpo, a Chicago artist, was presented by Professor Anton J. Carlson, of the University of Chicago, and accepted by Dr. William F. Petersen, chairman of the Board of Governors. Brief addresses were made by Dr. James B. Herrick, also a founder of the Institute of Medicine and for fifty-seven years a close friend of Dr. Hektoen, and by Dr. Christian Bay, librarian of the John Crerar Library.

DR. WALTER B. CANNON, George Higginson professor of physiology emeritus of the Harvard Medical School, has been elected a member of the Mexican Society of Natural History. Dr. Cannon is now carrying on physiological research work at the National Institute of Cardiology in Mexico City, where it is expected that he will remain for about three months.

THE following members of the department of botany of Michigan State College will retire next summer: Dr. Richard de Zeeuw, professor of botany, who has been at the college since 1909, and Dr. H. T. Darlington, associate professor of botany, who has been at the college since 1914. Dr. Ernst A. Bessey will relinquish his administrative work as head of the

partment on September 1 and for a year will continue in research work with the title of distinguished professor. Dr. F. L. Wynd, assistant professor of tany at the University of Illinois, has been appointed professor of botany and chairman of the partment for the coming year.

DR. FRANK HOVORKA, professor of chemistry at Western Reserve University, has been appointed acting head of the department of physics to succeed Dr. Harry W. Mountcastle, who is retiring in June.

DR. ALBERT D. KAISER, since 1931 associate professor of pediatrics at the School of Medicine of the University of Rochester, has been appointed professor f child hygiene. He has also been appointed health officer of the City of Rochester to succeed Dr. Arthur I. Johnson, who is retiring.

DR. ALBERT S. THOMPSON, instructor in psychology t the University of Pennsylvania, has been appointed associate professor of psychology at Vanderbilt University.

DR. WILLIAM D. GRAY, of Miami University, now associate chief in the biological laboratory of the U. S. Quartermaster Corps, has been chosen associate professor of botany at Iowa State College. He will begin service on release from his present position. Charles A. Bower, assistant professor of soils at the college, will join the U. S. Bureau of Plant Industry, Soils and Agricultural Engineering. His headquarters will be at Riverside, Calif.

DR. CHARLES LOEWNER, of Brown University, has been appointed associate professor of mathematics at Syracuse University, beginning on September 1.

DR. EWING C. SCOTT, head of the department of chemistry at Sweet Briar College and chemical adviser to the U. S. Tariff Commission, has been appointed associate professor of chemistry at Syracuse University. He succeeds Dr. Albert L. Elder, who has become director of research for the Corn Products Refining Company.

D. S. A. ADAMS, who has been teaching biology at Rugby School, England, has been appointed professor of chemistry at Ghazi College, Kabul, Afghanistan.

LIEUTENANT COLONEL BASIL C. MCLEAN, M.C., Surgeon General's office, who was released to inactive status in November, has taken up his work as director of the Strong Memorial Hospital of the University of Rochester. Dr. McLean has been appointed by Governor Dewey to serve as chairman of the Temporary Commission on Medical Care, the purpose of which is "to make necessary studies, to devise programs for medical care for persons of all groups and classes in the State of New York."

BELL TELEPHONE LABORATORIES has announced that Dr. R. R. Williams, chemical director, has been appointed chemical consultant, in accordance with his expressed desire to be free to devote more time to matters of national interest in the field of nutrition. Dr. R. M. Burns, hitherto assistant chemical director, has been appointed chemical director, in charge of the chemical laboratories.

DR. HAROLD E. THOMAS, associate plant pathologist in the University of California at Berkeley, has been appointed director of the Strawberry Institute, recently founded by the industry to carry on research in strawberry breeding near San Jose, Calif.

CAPTAIN WILLIAM S. MCCANN, MC-USNR (inactive), has resumed his work as Dewey professor of medicine at the School of Medicine of the University of Rochester as of November, 1944, after serving two years in the Navy.

DR. FRANK A. HARTMAN, professor of physiology at the Ohio State University, spent five weeks recently at the Archbold Biological Station at Lake Placid, Fla., collecting the adrenals and thyroids of birds for a comparative study of their histology.

DR. CLAUDE E. ZOBELL, associate professor of microbiology at the Scripps Institution of Oceanography, gave on April 25 the annual William Conger Morgan Memorial Lecture under the auspices of Phi Lambda Upsilon at the University of California. His subject was "The Role of Bacterial Activity in the Formation and Transformation of Petroleum Hydrocarbons." For several years the American Petroleum Institute has sponsored a research project on this subject under the direction of Dr. ZoBell.

PROFESSOR W. F. LOEHWING, of the department of botany of the State University of Iowa, addressed the Kansas State College Chapter of Gamma Sigma Delta (honorary agricultural fraternity) at its annual initiation meeting on the evening of April 14 on "Root Interactions of Plants." He also addressed the annual meeting of the Kansas Academy of Science at Manhattan, Kansas, on April 14, where he spoke on "Recent Advances in the Plant Sciences."

DR. LIONEL S. MARKS, professor emeritus of mechanical engineering at Harvard University, will give three lectures on "Rockets, Gas Turbines and Jet Propulsion," their history, principles, present use and future development, in Ohio and Pennsylvania during May. The lectures will be sponsored by the American Society of Mechanical Engineers, and will be open to the public.

DR. NEIL STEVENS, of the department of botany of the University of Illinois, addressed on May 4 a dinner meeting of the University of Kentucky Chapter

of Sigma Xi. His subject was "What It Takes to Teach the Plant Sciences." Dr. Alfred Brauer was recently elected president of the chapter to serve during 1945–46.

THE Chemical Institute of Canada, which now combines the aims and activities of most of the previously existing chemical groups in Canada, plans to hold a conference at the Chateau Frontenac Hotel, Quebec, on June 4, 5 and 6. The program includes the celebration of the twenty-fifth anniversary of the opening of the department of chemistry of Laval University; technical sessions on pure chemistry, biological chemistry, agricultural chemistry and nutrition, chemical education, chemical engineering, rubber and plastics, textile chemistry and protective coatings; and a symposium on the "Coordination of Chemical Research and the National Welfare."

THE Child Health Program under the direction of Dr. Arild Hansen, of the department of pediatrics at Galveston of the University of Texas, in cooperation with related organizations held on March 9 a Pediatric Conference on psychologic and psychiatric problems in children. The guest speakers were Dr. James S. Plant, director of the Essex County Juvenile Clinic, Newark, N. J.; Dr. Milton E. Kirkpatrick, director of the Guidance Center of New Orleans, and Dr. John H. Waterman, director of the Guidance Center of Houston.

A GRANT of $282,000 for studies of genetic factors of intelligence and emotional variation in mammals for a five-year period has been made by the Rockefeller Foundation to the Roscoe B. Jackson Memorial Laboratory. The work will be under the general direction of Dr. C. C. Little, director of the laboratory, and will for the most part be carried out at Hamilton Station, a fifty-five acre tract of land and buildings at Salisbury Cove, Maine, which is near the main laboratory at Bar Harbor. It is planned to use dogs for most of the study, although experiments will also probably be conducted with rodents and certain of the smaller farm animals. A long-time program will be planned. The Board of Directors of the American Kennel Club have expressed willingness to cooperate in the work and to help with records and by interesting the breeders of thoroughbred dogs throughout the country. No announcement of the staff will be made at present pending a careful preliminary study and period of planning the program.

THE Jessie Horton Koessler Fellowship of the Institute of Medicine of Chicago for the aid of research in biochemistry, physiology, bacteriology or pathology will be available on September 1. The stipend is $500 a year with the possibility of renewal for one or two years. Only such applications will be considered as are approved by the head of a department in the field mentioned or by the director of a research institute or laboratory in Chicago, and it is stipulated that the recipient of the fellowship shall be given adequate facilities for carrying out the proposed research, concerning which full information is required in the application. Applications will be received up to July 1 and should be sent to Dr. Paul R. Cannon, chairman of the Committee on the Jessie Horton Koessler Fund, 950 East 59th Street, Chicago 37. Since there are no formal blanks, application should be made by letter.

THE *Journal* of the American Medical Association states that the Rockefeller Foundation has given to the School of Medicine of the University of Pennsylvania funds to provide post-war training at an advanced level for a number of young medical men of exceptional promise whose medical education has been interrupted by the war and who now are in the armed forces. The men will be selected for study and work under distinguished teachers in surgery, pharmacology or psychiatry, the foundation having made three grants of $8,000 to provide the training in each of these fields. The training, which will begin after the men have concluded their military service, will cover a maximum of four years, and the number of recipients will depend on the extent and character of the instruction required.

IT is reported in *Chemical and Engineering News* that the British Imperial College of Science and Technology has issued a booklet containing the proceedings of the conference of its 184 industrial representatives, 129 teaching staff and senior students and several governors of the Imperial College. During the conference, held under the auspices of the Vacation Work Committee, two sessions convened, one on "Postwar Technical Requirements in Industry," and the other on "Postwar Requirements in Scientific Education."

AT the recent ceremony in the Hall of the Royal Society of Medicine, London, presentation to the society was made of a talking film projector, a gift from the American Society of Anesthetists in recognition of the friendly relations which the associations of the war have accentuated between anesthetists of these allied peoples. After the handing over of the apparatus it was used for the first time in showing an American medical film, a colored sound film of United States children being tested for deafness. The projector was presented by Colonel Ralph M. Tovell, consultant in anesthesia to the chief surgeon of the American Expeditionary Forces in Europe. It was accepted on behalf of the Royal Society of Medicine by the president, Surgeon Rear-Admiral G. Gordon-Taylor, and the president of the section on anesthetics, Dr. Francis Evans.

DISCUSSION

[N]EWLY DISCOVERED PERIODICITY OF 16 MONTHS IN THE SUN'S WAVE RADIATION

[In] Volume 6 of the *Annals* of the Smithsonian [Astro]physical Observatory we disclosed 14 regular [perio]dicities. Their summation, as plotted in Fig. 14 [of *A*]*nnals* 6, makes up very nearly exactly the varia[tion]s of the sun's emission of radiation, so far as such [vari]ation appears in monthly mean values of the "[sola]r constant" of radiation. All these 14 periods [are] approximately aliquot parts of 273 months, or [22¾] years. This is approximately double the length [of t]he sunspot cycle, and corresponds to Hale's mag[neti]c cycle in sunspots, as well as to a period found [by] meteorologists in weather, and by Douglass in [wid]ths of tree rings.

[M]any meteorologists, and notably Clayton, have [mad]e use of the variation of sunspot numbers, or of [sun]spot areas, as a supposed measure of solar varia[tion]. Strangely, however, we could find no sure indi[cati]on of a periodicity approximating 11.3 years in [the] variation of the solar constant of radiation. We [so s]tated in Volume 6 of the *Annals*. Several per[sons] have brought this curious absence of a period of [136] months to my attention. Some have even re[flect]ed a little on the accuracy of our more recent [sola]r constant measurements, because the sun-spot [peri]od of variation does not seem to appear in them. [Tha]t period was indeed reported in our Mount Wilson [wor]k in the *Annals,* Volume 4, but possibly those indi[cati]ons may have been caused by changes in sky trans[pare]ncy at Mount Wilson. We now occupy at Monte[zum]a, Chile, a much better station than Mount Wilson [as r]egards sky conditions, and have improved our [met]hods of observing. We can not willingly adopt [the] deprecatory view of our recent work, which com[pris]es nearly 20,000 solar constant values, made under [such] conditions.

[T]he matter was brought sharply to my attention [by] Dr. Schell, of Harvard University, on April 4. [Sinc]e then Mr. Aldrich, acting director of the Astro[phy]sical Observatory, and others of his staff, have [bee]n more carefully searching our solar constant re[sult]s for some vestige of an 11.3-year periodicity. A [pap]er on their findings will probably issue later.

[It] occurred to me that a study of the column headed ["D"] or "B–C" of Table 32 of Volume 6 of the *Annals* [migh]t to reveal the 11.3-year period, if existing. This [colu]mn gives the residuals remaining when the observed monthly mean values of the solar constant are subtracted from the monthly summations of the 14 known periodicities above referred to.

As a measure tending to eliminate accidental errors of observation, I first computed 5-month running means of the column "D." By adding to the values given in *Annals* 6, results of more recent work, as yet unpublished, I had somewhat more than two complete 11.3-year cycles. The earlier work, 1920 to 1930, yielded a fairly definite indication in these data of a cycle of about 11.3-years, indicating a minimum of the solar constant due to sunspots about the year 1925 or 1926. The amplitude of this cycle is not quite 0.1 per cent. of the solar constant. A second group of smoothed values, of the years 1931 to 1941, was partly of the same trend as the first, but at the latter end inconsistent. However, conclusions should be reserved until the publication of the investigation which Mr. Aldrich and his assistants are now making.

It will be asked by some: If only a trifling (1/10 per cent.) indication of the influence of the sunspot cycle, which has an amplitude of over 100 sunspot numbers, is found in the variation of the sun's output of radiation, how is it that well-recognized meteorological changes are closely in correlation with small sunspot variations? I suggest: It is well known that the sun, like a machine gun, especially in sunspots, bombards the earth, and probably all space, with electric ions. These objects, encountering the earth's atmosphere, further ionize it. Electric charges, as well known for nearly a century, act as centers for the agglomeration of dust and water particles. Thus increased solar activity in the nature of ionic discharges tends to increase haze and cloudiness in the earth's atmosphere. Such obstructions would absorb solar radiation. Thus the atmosphere would be heated when solar bombardments increase. Other meteorological consequences would naturally follow. Again, it may be that 11.3-year periodic fluctuations of the sun's extreme ultra-violet radiation, cut off by ozone in the upper atmosphere, may be many times 1/10 per cent. In such ways the sunspot cycle, and its details of sunspot variation, might have meteorological importance, without being associated with considerable fluctuations of the sun's total output of wave radiation.

But this is not the subject announced in my title. When I had smoothed the residual values "D," or "B–C," of Table 32 of *Annals* 6, and had plotted the 5-month running means, I perceived a saw-tooth appearance of great regularity. It seemed to have about

15 months period. I tabulated the values by successive lines of 15 months in length, and took means. The means of the columns indicated an irregular periodic fluctuation of about 0.0005 calorie in amplitude. As all the 14 periodicities enumerated in Table 31 of *Annals* 6 are nearly aliquot parts of 273 months, I thought it would be better to retabulate the values for a period of $\frac{273}{18}$ or 15.2 months. The resulting curve of this period was smoother than that for 15.0 months, and had a slightly larger amplitude. It then occurred to me to try a period of $\frac{273}{17}$, or approximately 16.0 months. And now I obtained the following series of mean values of the tabulation. The numbers below are given in units of $\frac{1}{10,000}$ calorie.

Month	1	2	3	4	5	6
Values	−62	−74	−74	−118	−158	−154
Month	7	8	9	10	11	12
Values	−180	−162	−144	−92	−70	−44
Month	13	14	15	16		
Values	−14	+40	+48	+13		

This defines a curve, which, as the reader may see by plotting the values, is very smooth, has its maximum at month 15, which corresponds to June, 1921, and minimum at month 7, which corresponds to November, 1920.

I have recomputed the 16-month period from unsmoothed values of the residuals "D." A slightly different and less perfect curve of about the same amplitude resulted. Recalling that "D" stands for *synthetic minus observed* solar constant values, and giving partial weight to the phases found in computations from unsmoothed data, I now set the initial dates of maximum and of minimum of the solar constant for the 16-month periodicity at October, 1920, and May, 1921, respectively. The amplitude, 0.00228 calorie, is 0.12 per cent. of the solar constant. This amplitude gives the new 16-month periodicity a standing of 1.7 times the importance of the periodicity of 9.79 months, and 1.3 times the importance of the periodicity of 8⅛ months, as they are listed in Table 31, *Annals* 6.

C. G. ABBOT

SMITHSONIAN INSTITUTION

QUININE FROM REMIJIA BARK

A REPORT on cinchona exploration in South America recently appeared in your columns.[1] In this, surprise was expressed at finding in the bark of *Remijia pedunculata* "up to 3 per cent. of quinine sulfate (*sic*) with very little admixture of other alkaloids."

I should like to direct attention to the well-documented fact that this and related species of *Remijia* have for about seventy-five years been known to be quininiferous.[2] Indeed, for several years beginning in 1879 many thousands of tons of the bark of these trees were exported to Europe for the extraction of quinine. Most went to England, some being transshipped to the Continent. F. A. Flückiger states that in 1881, out of 100,000 bales (*surons, colli*) of quinine-containing barks shipped into London, 60 bales of 50 kilos weight each consisted of "Cuprea Bark" (*Remijia* species), or a total for that one year alone of 3,307 tons. Of the approximately seven and a half thousand tons of bark shipped from northern South America in 1881, cuprea bark was the chief part.[4]

It appears that after several years the trade in cuprea or *Remijia* bark waned as a result of depletion of readily available forests. Thus, in the course of a comparatively few years, little heed was paid to this once important botanical raw material until the exigencies of war have again focussed attention on it.[5]

Species of *Remijia* were introduced into India to furnish raw material to the quinine industry (Sikkim plantations, *ca.* 1888).[6]

GEORGE M. HOCKING,
Chief Pharmacognosist

S. B. PENICK AND COMPANY
NEW YORK, N. Y.

CENTENNIAL OF WOOD'S "CLASS-BOOK OF BOTANY"[1]

THE year 1870 was not only the birth year of the Dartmouth Scientific Association but also the twenty-fifth anniversary of an event closely associated with the scientific interests of Dartmouth. The year 1945 is therefore the centennial of that scientific event—the publication of the first edition of Wood's "Class-Book of Botany" at Claremont, N. H. Before the end of its usefulness, this famous text-book and manual had gone into its fiftieth edition and been sold to over hundred thousand students.

Dartmouth has a double claim for recognition of its contribution to the development of this book—the first botany text to be approved by the American pu

[1] W. C. Steere, SCIENCE, n.s., 101: 177–8, 1945.

[2] F. A. Flückiger, *Vorwerks Neues Jahrb. f. Pharm. u. verwandte Fächer*, 36, 1871.

[3] "The Cinchona Barks," p. 52, 1884.

[4] *Ibid.*, p. 55.

[5] D. Howard and J. Hodgkin, *Pharm. Jour.*, (3) 578–9, 1881; *idem*, *Jour. Chem. Soc.*, 41: 66–8, 1 Whiffen, *Pharm. Jour.*, (3) 12: 497, 1881; Triana, *de Pharm. et de Chim.*, (5) 5: 565–75, 1882; Ar *ibid.*, (5) 5: 560–4, 1882; G. Planchon, *Jour. de Ph et de Chim.*, (5) 10: 329–336, 419–432, 1884; W Dictionary of the Economic Products of India, II, 316. *ca.* 1896.

[6] Watt's Dictionary of the Economic Products of In II, pp, 314, 5.

[1] Read at the meeting of the Dartmouth Scientific Association on March 21, 1945.

In the first place, the author was a Dartmouth graduate, and, secondly, he collected the materials for the book in the vicinity of Hanover and with the active assistance of a member of the Dartmouth faculty.

Alphonso Wood was graduated from Dartmouth in 1834, with Phi Beta Kappa rank. He had been born in Chesterfield, N. H., in 1810, educated in the schools and academy there and, like many students of his time, had taught in the rural schools throughout his college course. At Dartmouth there had been no formal training in science, but he had learned something about plants through contacts with lecturers and students in the Medical School, where biology was recognized as an important science.

After graduation he became a teacher of Latin and natural history at Kimball Union Academy, only thirteen miles from Hanover. There he found his greatest interest to be in plants and the teaching of botany to the coeducational student body. Following his marriage in 1842, his wife encouraged this special interest and he gave ever greater attention to the subject with emphasis on field botany and the study of living plants.

In the same year, Dr. Edward E. Phelps, of Windsor, Vt., became lecturer in the Dartmouth Medical School, driving back and forth, sometimes by way of Meriden. This famous doctor and teacher taught the Materia Medica, had done special work in botany and had collected his own herbarium. Just how much he helped the teacher at Meriden, we do not know, but Wood put Dr. Phelps first in the preface acknowledgments of his new "Class Book of Botany."

This book was remarkable for its origin as well as for its immediate success in competition with other texts. It was written because Wood, the obscure teacher, was dissatisfied with all books prepared by professional botanists. The most eminent of these authors was Asa Gray of Harvard, Fisher professor of natural history, although born in the same year as Alphonso Wood, then only thirty-four years old. Gray's "Botanical Text-Book" of over 500 pages and a thousand wood engravings was written by America's greatest botanist, then and still. In 1842 it was in its second edition, designed for "colleges, schools and private students" and published by the powerful house of Wiley and Putnam.

Early in 1844, Wood went to Cambridge and asked Professor Gray to prepare a botany text that could be used to better advantage in the many schools like Kimball Union Academy. Gray replied that there was no need for such a book—that the academy teacher should be able to use the books on the market. After trying again to get along with them in the spring of 1844, Wood approached Dr. Gray a second time and tried to state his objections to current texts in botany. Failing to arouse Gray's interest in writing a new book, Wood determined to prepare his own text.

The new book was printed privately in the following year, a well-bound, full-size, illustrated text of 475 pages but in an edition of only 1,500 copies. It was sold out immediately, and a second edition of 3,000 copies was at once produced through a Boston publishing house. It displaced older books on its merits alone, since the author remained at Meriden, improving the text, correcting errors and adding to the manual part of the book, since the descriptions of native plants formed the core of it and made it unique and attractive to teachers.

For this first edition, three fourths of the species, and later more, were described from specimens, many collected near Meriden, some from the herbarium of one Abel Storrs of Lebanon, N. H., and others from Dr. Phelps's collection at Windsor. Later Wood traveled extensively to learn plants in other states, even as far as the Pacific Coast. On one such trip in August, 1866, he and the Reverend G. H. Atkinson (Dartmouth, 1843), climbed Mt. Hood in Oregon, the first white men to reach its summit. In New England he took a particular interest in its alpine and sub-alpine flora and discovered many of the stations for these rare plants, including the famous area at Lake Willoughby in Vermont.

From the teacher's viewpoint, he sought to have his book appeal to the reason of the student, rather than to his powers of memory. It's still a good idea. The following paragraph from the first edition's preface indicates other ideals:

That there is need of a new Class-Book of Botany, prepared on the basis of the present advanced state of the science, and, at the same time, adapted to the circumstances of the mass of students collected in our institutions and seminaries of learning, is manifest to all who now attempt either to teach or to learn. The time has arrived when Botany should no longer be presented to the learner encumbered with the puerile misconceptions and barren facts of the old school, but as a System of Nature, raised by recent researches to the dignity and rank of a science founded upon the principles of inductive philosophy. . . . That theory of the floral structure which refers each organ to the principles of the leaf, long since propounded in Germany by the poet Goethe, and recently admitted by authors generally to be coincident with facts, is adopted, of course, in the present work.

For all these and other points of improvement thought to be incorporated in the new book, Wood remained modest about his project. He frequently emphasized that his book was elementary and referred the reader to Gray's books for complete details of topics. On the difficult point of correct scientific

names for plants, he adopted those given by Torrey, Gray and others "for very obvious reasons." He always maintained this courteous and respectful attitude toward Gray in spite of their rivalry. He was content to be a good teacher and to make good money from his various books, of which about 800,000 copies were sold.

If there was any one reason for the wide sale and popularity of Wood's "Class-Book of Botany," it was the provisions he made for its use in identifying native plants by quick, easy methods. These were not found in earlier books. For this reason the new book was a great stimulus to field botany and observations of living plants. Wood's great practical contribution to the technique of rapid identification was the scheme he called analytical tables, now known as keys. In his preface, Wood gave Dr. Phelps much credit for the idea, but they were first published and later improved in the "Class-Book." They were both new and useful, just the tools needed by the amateur. The professionals had similar schemes based on natural affinities between families and genera but very difficult for use by others or in the field. They still are and they are still printed in most sections of Gray's "Manual," though many of us would like to see the Woods-Phelps type of artificial keys in the next edition. It's about time after a long one hundred years.

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SCIENCE AND THE NEW DRAFT REGULATIONS

In recent articles in Science (101: 172–173, 1945), and in *The Scientific Monthly* (LX, 37–47, 1945), Dr. M. H. Trytten, director of the Office of Scientific Personnel of the National Research Council, has forcefully pointed out that our present manpower policies have endangered the postwar supply of scientists. The drastic decline in graduate students and in the number of doctoral degrees that have been granted during the war years doubtless will seriously affect the future of American science.

At this moment, an even more serious threat is taking place which will still further curtail the supply of scientific personnel. I refer to the new Selective Service policies promulgated in *Local Board Memorandum No. 115,* as amended on February 21, 1945. Under these new regulations, a considerable number of war research workers and probably the major portion of university staff members who are in the 18 to 30 age group will be reclassified and inducted into military service—most likely for combat duty. According to the above memorandum, it is also expected that the 30 to 38 age group will follow soon thereafter.

Certain agencies, such as the National Roster and OSRD, are authorized to certify research workers for deferment by the local boards. However, the above memorandum states that these agencies ". . . have agreed to specific limitations upon the total number of certifications that will be made . . . and definite limitations upon the type of persons to be certified. . . ." According to reports received by the American Association of Scientific Workers, the universities and colleges, at the insistence of the manpower authorities, have made up lists designating which members of their staffs are first to be released for induction.

Unless these steps are halted, scientific personnel on college staffs and on research projects of less immediate importance to the prosecution of the war will shortly be swept into the armed forces. In terms of manpower, the total number of people involved is small. Induction or deferment of these groups of scientists can do little, therefore, to affect the requirements of the armed forces. In terms of the loss to society and to science, however, the induction of these younger scientists will bring about a grave situation. It will deprive society and science of a group which is probably at the height of its originality and promise. It will furthermore seriously curtail the teaching facilities of the colleges, and thus bring about a still greater deficit in the postwar supply of scientists than even the alarming situation forecast by Dr. Trytten.

There is considerable irony in this new threat to scientific personnel. The contributions science has made to the war effort have impressed the public and our national authorities with the need for fostering and expanding postwar scientific development. This is exemplified in President Roosevelt's letter recently to Dr. Vannevar Bush. Furthermore, the current plans for expanded national and international economies, such as those embodied in the President's program for 60 million jobs, and in the plans of the Dumbarton Oaks, Bretton Woods and Yalta agreements, carry with them a demand for an increased number of scientists, technologists and teachers. At the same time that these important new plans are being developed, young scientists are being drained away and our capacity to provide new ones is being destroyed.

The new Selective Service regulations (*l.c.,* p. 1) that deferments may be made by local draft boards, if it is shown that individuals are "irreplaceable . . . in support of the national health, safety or interest." Scientists will agree that the group of their younger colleagues clearly falls into this category and that all steps should be taken by colleges, universities and other employers of scientists to obtain deferments for this small but important group.

Because we believe that it is clearly in the national

interest to defer the young scientists who are working in the universities and on research projects not immediately vital to the war effort, the American Association of Scientific Workers has made representations to War Manpower Commissioner McNutt, Selective Service Director Hershey and to various authoritative scientific bodies. It is important, however, that a wider protest be made through the other scientific societies, through colleges and universities and by individual scientists.

The AAScW is also preparing a detailed memorandum to the Selective Service System pointing out the importance of deferring research and teaching scientists, as it pertains to the future of the national well-being. We invite other scientific societies, colleges and universities to join us in memorializing the Selective Service to preserve the activities of scientific personnel in the national interest.

HARRY GRUNDFEST,
National Secretary,
American Association of Scientific Workers
PRINCETON UNIVERSITY

SCIENTIFIC BOOKS

THE CLIMATE OF INDIANA

Climate of Indiana. By STEPHEN S. VISHER. 511 pp. 492 figures. 81 tables. Indiana University. 1944.

THIS is by far the most comprehensive and complete climatological history compiled for any State. It embodies unique features not ordinarily found in works of this kind, among which may be mentioned a well-deserved recognition of the services of the climatological observers of the Weather Bureau whose unselfish devotion to their observational work, often for long periods of time, makes possible such valuable publications as here presented.

These thousands of public-spirited men and women, instead of asking the all-too-frequent question "What is there in it for me?", are content with the conscious satisfaction of a public service faithfully rendered to their community, State and nation, not only for its current usefulness, but also to be left as a priceless heritage to generations yet to come.

Recently Dr. Isaiah Bowman declared, "Facts more valuable than all the gold in the Klondike lie hidden in the climatological records of the Weather Bureau." Dr. Visher has not only brought to light many of these facts that had lain dormant in the basic data for Indiana, but has given due credit to their source. The records show that for this State 39 observers have served, past and present, for periods ranging from 20 to 60 years, and Indiana until very recently had the dean of the some 5,000 for the United States, Mr. Elwood Kirkwood, Mauzy, with a record of more than 60 years. Mr. Kirkwood passed away a few months ago.

The first chapter of Dr. Visher's book contains a general summary of Indiana's climate, followed by discussions of the several climatic elements, profusely illustrated by maps and graphs with a minimum of tabular matter. Many of the illustrations have to do with variations from the standard normals which bring out graphically pertinent facts in anomalies and the "to be expected" frequencies of significant and important weather occurrences. This is the outstanding recommendation for the book.

Supplementing the basic data are many auxiliary maps and graphs which afford convenient "Weather Guides," valuable in long-time planning for agriculture and other enterprises. Among such numerous maps the following may be mentioned as illustrations of their general character:

The lowest temperature of record in 80 per cent. of the years, that is, only one year in 5 has experienced lower temperatures than those given.

The average annual number of cold days, with subfreezing daily normal temperature; moderately warm days 50–68°, and hot days, daily normals 75° or higher.

Dates of beginning and ending of summer, based on daily normal temperature of 68°.

Average depth of frost penetration.

Number of days per decade with temperature continuously below 10°, 20°, and the lowest for the coldest month of the year in 20 per cent. of the years. That is, in 80 per cent. of the years the temperature did not go lower than those shown on the map.

Several maps show various rainfall intensities, such as the percentage of years with 3 or more inches in 3 successive days.

In many cases data, both temperature and precipitation, are given for pairs of successive months, supplementing the usual seasonal (3-month) maps. This device is used also in drought summaries, such as rainfall totals for the driest pair of months during the crop-growing season.

Several maps show maximum and minimum values of data that are exceeded in a relatively small percentage of the years, such as dry months for which the values given are exceeded for dryness in only 20 per cent. of the years. That is, a drier month may be expected, on the average, only one year in 5.

An interesting map shows drought frequency in

terms of the sum of the percentage of normal rainfall for each of the 3 summer months (June to August) when each receives less than 1.5 inches.

In addition maps are included showing the average dates of planting and harvesting important crops in Indiana and the temperature relation to these dates in its annual march.

In brief, the book is outstandingly complete in subject-matter and profusely illustrated, containing nearly 450 climatic maps for Indiana, in addition to many other forms of graphic presentations, the greatest number ever published for any State. Among the some 80 tables of climatic data, detailed weather records for long periods of time are given for key Weather Bureau stations representing different areas of the State. Most of the maps could well have been in larger scale, but this, in view of their great number would have increased greatly the size of the volume. However, if this had been possible, it would have been well worth while. Dr. Visher truly has presented a challenge to climatologists of other States as a guide for future studies and model for publications of like character.

J. B. Kincer

REPORTS

TECHNOLOGICAL MANPOWER

Dr. Charles L. Parsons, secretary of the American Chemical Society, has addressed the following letter to the President of the United States:

We appeal to you for aid to forestall disaster. England, Russia, Belgium, Canada, and even France, have already acted. Only the United States fails to realize that the elimination of technological brains—the "know how" of production, the source of progress, and the foundation of our success in the world's future economy—can only lead to catastrophe.

The training of chemists, chemical engineers, physicists and other indispensable scientists has virtually ceased. At least 50 per cent. of our technological manpower is under thirty years of age. The younger scientists are already in the Army. Those ready for our colleges are not permitted to train to enable America to compete in the peace to come. England, Canada and Russia, per contra, are crowding their technological schools for this competition; some are even doubling their attendance.

They are allowing virtually none to leave production for their combat forces. Our own production is already decreasing and will become stagnant for lack of this type of man, one of whom can make jobs for many. They have been trained to use brains, not arms. The combat army would be strengthened by their discharge and efficient utilization. Modern progress and industrial competition are impossible without them. Research is their tool. Their output has made this nation strong and will assure its future if permitted to function.

American technology has given birth to the greatest power of all time. To-day we are drying up prosperity at its source. Public opinion of the future will view with amazement the waste of scientists in World War II, will applaud the unequaled accomplishments of the few who were utilized, and will condemn the lack of trained personnel in the economic competition that is to come. Our children and grandchildren will not forgive the loss of an entire generation of scientists—a disaster that can easily be avoided.

No more than 100,000 of the 10,000,000 in the combat services are involved in the problem. Comparatively, their number is insignificant. Before induction they already have saved this war by enabling America to keep abreast, and often ahead, of the miraculous devices of our enemies. They have admirably demonstrated that "Science is Power."

Mr. President, only you can avert a national tragedy. We ask that technological brains may still grace our colleges and save our production; that early discharge come to those in the services. We are prepared to prove our thesis before any unbiased jury you may appoint. We especially urge the early discharge of technological men.

Dr. Parsons also made public an appeal which he has sent to the 40,000 members of the American Chemical Society, urging them to use their influence individually to save America and American industry from disaster. From the inception of the Selective Service law every effort has been made by the society, working through administrative channels, to see that chemists and chemical engineers were utilized where they might serve America best—in the appropriate armed services, in the "production army" and in research essential thereto. The appeal reads:

With the exception of those individuals who through misguided patriotism felt that it was essential to be in uniform irrespective of the efficient utilization of their specific training and experience, the society's efforts in cooperation with Selective Service until March, 1944, were highly successful.

The virtual blanket draft of men 18 to 26 years of age, later extended to 18 to 29 years of age, has entirely altered the picture so that America faces a future, which, when carefully surveyed, is little less than appalling. All efforts to obtain real relief through administrative procedure have failed. We regret, deeply regret, that there appears to be no way to save the situation except through public opinion and legislative relief.

The McDonough bill now has been introduced into Congress by Congressman McDonough, of Los Angeles, calling for legislative relief in the hope that America's future during the present conflict and in the postwar world may be conserved. We are asking every member of the Amer-

can Chemical Society, and industrial leaders who are especially interested in the outcome, to read and study carefully the data which the society has assembled on scientific and technological manpower, and having done so to express their views to their Congressmen and to their Senators in order that their representatives may have the reaction of those especially qualified to advise them in this matter. They will read and study your letters especially if you are or are to become a veteran.

Your officials are doing everything in their power to remedy the situation. The public must be aroused. Without the aid of those who will suffer most from the loss of an entire generation of scientists, we are helpless. Please do your duty as you see it.

SPECIAL ARTICLES

GROWTH-RETARDING EFFECT OF CORN IN NICOTINIC ACID-LOW RATIONS AND ITS COUNTERACTION BY TRYPTOPHANE[1]

IN a previous study,[2] it was shown that corn or corn grits exert a pronounced growth-retarding effect in rats on nicotinic acid-low rations and that this untoward effect can be completely counteracted by including 1 mg of nicotinic acid per 100 gm of ration. At the same time, it was reported that raising the level of casein modified the action of corn. This report is an elucidation of that observation.

The basal ration used had the following composition: Labco casein (3 times extracted with 95 per cent. ethanol) 15, sucrose 78, corn oil 3, salts IV[3] 4 and cystine 0.15 parts. Vitamins were incorporated in the ration at the following levels: thiamine 0.2, riboflavin 0.3, pyridoxine 0.25, calcium pantothenate 2.0, choline chloride 100, inositol 10, 2-methyl-naphthaquinone 0.1 and biotin 0.01 mg per 100 gm respectively. Halibut liver oil (diluted 1:2 with corn oil) was fed at a level of 2 drops per week, with α-tocopherol included at 0.5 mg per drop. A norite eluate of solubilized liver extract, prepared so as to contain practically no nicotinic acid, was fed, where indicated, at a level equivalent to 11.5 μg B_c (*S. lactis* assay) per 100 gms of ration. These vitamin levels were maintained both in the basal and corn-supplemented rations and the nicotinic acid content of the basal ration was < 0.01 mg per 100 gm.

The low protein (L.P.) basal ration contained 15 per cent. casein and the high protein (H.P.) 20 per cent. casein. In all cases, corn was incorporated so as to replace 40 per cent. of the entire ration, which reduced the casein levels of the L.P. and H.P. rations to 9 and 12 per cent. respectively. Whole yellow corn meal and corn grits at a level of 40 per cent. added 3.4 and 3.6 per cent. of crude protein (N × 6.25), respectively. Weanling male rats were used throughout and in all cases at least 3 animals were used per group. The growth results obtained on the two rations are shown in Table 1 and demonstrate that casein has a marked protective action.

Since the protective action of casein could not be explained on the basis of its nicotinic acid content, other possible factors were considered. Inasmuch as corn is deficient in the essential amino acids lysine and tryptophane, it seemed logical that the additional casein might be contributing these amino acids in

[1] Published with the approval of the Director of the Wisconsin Agricultural Experiment Station. This work was supported in part by a grant from the National Dairy Council, on behalf of the American Dairy Association. We are indebted to Merck and Company, Inc., Rahway, N. J., for the generous supply of crystalline B vitamins; to the Abbott Laboratories, North Chicago, Illinois, for the generous supply of haliver oil; and to the Wilson Laboratories, Inc., Chicago, Illinois, for the solubilized liver extract, fraction L.

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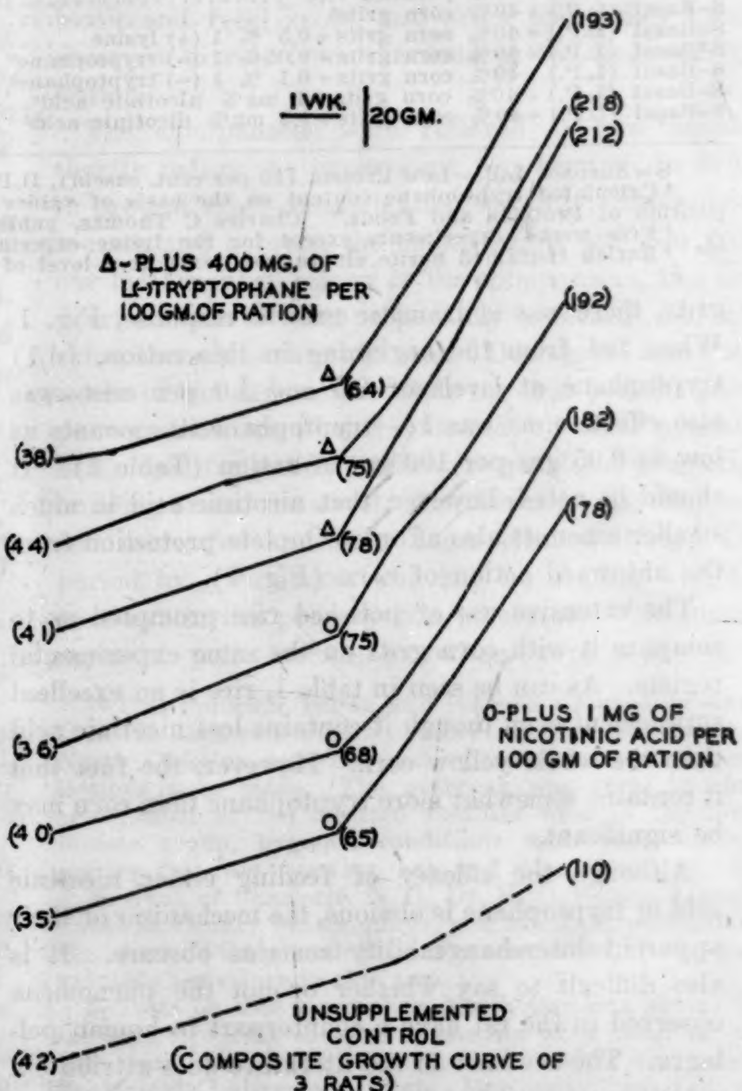

FIG. 1. Growth responses resulting from the addition of 1(-)tryptophane or nicotinic acid to the low casein plus corn grits diet and the growth curve of the unsupplemented control. (Figures in parentheses represent rat weights).

sufficient quantity to overcome the deficiency caused by corn. It was found that 1(+)lysine included in the ration at a level of 0.5 per cent. did not alleviate the deleterious effect of corn grits. This was not entirely unexpected, since even the low level of casein supplied almost enough lysine to satisfy the requirement indicated by Rose.[4] In concurrent experiments,[5] in which the low level of casein was replaced by purified proteins which contained more tryptophane than casein, corn grits did not produce a growth depression. When 1-tryptophane was added at a level of 0.4 per cent. to the low casein diet plus corn grits, there was a dramatic growth response, Fig. 1. When fed from the beginning in this ration, (d,1) tryptophane at levels of 0.5 and 1.0 per cent. was also effective, as was 1(−)tryptophane in amounts as low as 0.05 gm per 100 gm of ration (Table 1). It should be noted, however, that nicotinic acid in much smaller amounts also affords complete protection from the untoward action of corn (Fig. 1).

The extensive use of polished rice prompted us to compare it with corn grits on the same experimental régime. As can be seen in table 1, rice is an excellent supplement even though it contains less nicotinic acid than the whole yellow corn. However, the fact that it contains somewhat more tryptophane than corn may be significant.

Although the efficacy of feeding either nicotinic acid or tryptophane is obvious, the mechanism of their apparent interchangeability remains obscure. It is also difficult to say whether or not the phenomena observed in the rat have a counterpart in human pellagra. The evidence in the literature does attribute a role to protein deficiency in the etiology of pellagra, since Goldberger[6] found rather large amounts of milk and meat proteins to be of value in treating pellagrins. He also observed some beneficial results from tryptophane and cystine.[7] However, in 1925 Goldberger reported[8] that "it is possible that the P-P factor plays the sole essential role in the prevention (and thus the causation) of pellagra." The present report and previous studies show clearly that nicotinic acid is capable of playing "the sole essential role," but it is also shown that protein or tryptophane, particularly, may have a profound effect on the nicotinic acid requirement.

TABLE 1

EFFECT OF NICOTINIC ACID AND TRYPTOPHANE ON THE GROWTH OF RATS ON RATIONS CONTAINING CORN

Ration used	Total protein content (N × 6.25)	Tryptophane content[1]	Nicotinic acid content	Grams gained per week[2] and (range)
	%	mg%	mg%	gm/wk
S–Basal (L.P.)	15.0	180	< 0.01	29 (26-32
S–Basal (L.P.) + 40% yellow corn	12.4	128	0.92	13 (11-16
S–Basal (L.P.) + 40% yellow corn + 1 mg% nicotinic acid	12.4	128	1.92	32 (30-34
S–Basal (H.P.)	20.0	240	< 0.01	32 (31-34
S–Basal (H.P.) + 40% yellow corn	15.4	164	0.92	30 (22-35
S–Basal (H.P.) + 40% yellow corn + 1 mg% nicotinic acid	15.4	164	1.92	36 (33-38
S–Basal (L.P.) + 40% polished rice	12.0	138	0.57	31 (27-34
S–Basal (L.P.) + 40% corn grits[3]	12.6	118	0.27	7 (5- 8
S–Basal (L.P.) + 40% corn grits + 0.5 % 1 (+) lysine	12.6	118	0.27	9 (7-1
S–Basal (L.P.) + 40% corn grits + 0.05% 1 (−) tryptophane[3]	12.6	158	0.27	31 (27-37
S–Basal (L.P.) + 40% corn grits + 0.1 % 1 (−) tryptophane[3]	12.6	218	0.27	33 (26-35
S–Basal (L.P.) + 40% corn grits + 1 mg% nicotinic acid[3]	12.6	118	1.27	27 (25-29
S–Basal (L.P.) + 40% corn grits + 1.5 mg% nicotinic acid[3]	12.6	118	1.77	32 (30-34

S = Sucrose, L.P. = Low Protein (15 per cent. casein), H.P. = High Protein (20 per cent. casein).
[1] Calculated tryptophane content on the basis of values given by R. J. Block and D. Bolling in "The Amino Acid Composition of Proteins and Foods." Charles C Thomas, publisher, Springfield, Ill.
[2] Five weeks' experiments except for the lysine experiment, which was of two weeks' duration.
[3] Ration contained norite eluate (see text) at a level of 11.5 ug B_6 (*S. lactis* assay) per 100 gm of ration.

On the basis of studies with various carbohydrates,[9] and by direct examination of the intestinal flora,[10] strong evidence is at hand to indicate that the observations reported in the present study may be explained at least in part by extensive changes which occur in the intestinal flora.

Summary: Either 50 mg 1(−)tryptophane or 1.5 mg nicotinic acid per 100 gms of ration completely counteracts the growth retardation caused by the inclusion of 40 per cent. corn grits in a low protein ration. A possible explanation of this observation is discussed.

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POLIOMYELITIS VIRUS IN FLY-CONTAMINATED FOOD COLLECTED AT AN EPIDEMIC[1]

THIS paper is concerned with an experiment on the mechanism of spread of poliomyelitis. Its purpose is to report the detection of poliomyelitis virus in food exposed to flies at an epidemic in the summer of 1944. Much new evidence has accumulated within the past few years which suggests that the human alimentary tract (mouth and pharynx to colon) may be a portal of entry for the virus in human poliomyelitis.[2,3,4] Furthermore the virus has been repeatedly demonstrated in human stools,[5,6] in sewage,[7,8] and in flies,[9,10,11,12] but no direct evidence has yet been produced that fecal material, sewage or contact with flies on the part of the individual, his food or fomites, actually constitute links in the poliomyelitis infection chain.

It would be important therefore if it could be shown that food merely exposed to flies at an epidemic area is infective when ingested. The chimpanzee was selected to receive the exposed food because next to man this animal appears to be the most natural experimental host. The work of Howe and Bodian has proved not only that poliomyelitis virus given by mouth produces paralytic[4] and non-paralytic[13] infections in the chimpanzee, but also that these animals are susceptible to spontaneous infection.[14] They were therefore ideal test animals for this type of experiment in which as close an approximation to nature as practicable was desired.

Materials and methods: Although material was collected in several epidemic areas (North Carolina and New York) and at two camps in Connecticut during the summer of 1944, it is possible to speak with certainty of the results only after feeding the materials obtained in North Carolina.[15]

Flies were collected and fly-bait and food were exposed at 12, and food alone at an additional 8 homes of poliomyelitis patients within a week of the onset of illness. The food to be exposed was purchased at local stores and consisted of bananas, which were peeled and sliced on the spot to be studied, and sprinkled with a little sugar and water. One or two plates of food were exposed in and about the homes, usually in the kitchen and on the back porch, and the family was admonished not to touch them. The fly-bait, composed also of bananas and sugar plus liver or fish, likewise obtained locally, with added water to prevent desiccation, was placed beneath a fly-trap in the yard or on the back porch. The food and fly-bait were thus exposed for 24 to 48 hours, frozen on dry ice, transported to the laboratory and held in the frozen state until fed to the chimpanzees. In most instances there was gross evidence of fly contamination on both food and fly-bait in the form of vomit and fecal spots, and often many flies[16] were observed to rise from the food at the times of collection.

The chimpanzees were received as new animals shortly before the experiment was begun. In order to prevent cross-contamination not only from outside sources and between the chimpanzees, but also from our local monkey colony to the chimpanzees, two outdoor enclosures were separately screened and one chimpanzee was caged in each. During the first three weeks of the experiment while the first positive chimpanzee stools were being collected, all other primates being used for poliomyelitis were quartered in another building across the street. Furthermore, the chimpanzees were fed and their cages cleaned during this period by a caretaker who had no contact with the monkeys in the poliomyelitis laboratory. No human cases of poliomyelitis, moreover, were reported in

[1] Aided by grants from the National Foundation for Infantile Paralysis, Inc.

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[11] J. A. Toomey, W. S. Takacs and L. A. Tisher, *Proc. Soc. Exp. Biol. and Med.*, 48: 637, 1941.

[12] (a) J. D. Trask, J. R. Paul and J. L. Melnick, *Jour. Exp. Med.*, 77: 531, 1943. (b) J. D. Trask and J. R. Paul, *Jour. Exp. Med.*, 77: 545, 1943.

[13] D. Bodian and H. A. Howe, *Jour. Exp. Med.*, 81: 255, 1945.

[14] H. A. Howe and D. Bodian, *Jour. Exp. Med.*, 80: 383, 1944.

[15] This epidemic began and reached its peak in June, 1944, in Catawba County, where most of the cases in North Carolina occurred and where almost all the collections were made. The outbreak was rural in character, most of the affected families were in the lower income group, hygienic conditions were poor, outdoor privies the rule, weather hot and flies abundant. Dr. J. S. Gaul, of Charlotte, N. C., Dr. H. C. Whims, Lincoln-Catawba County health officer, and his staff, particularly Mr. Jack Wildey and Miss Frances Allen, R.N., gave valuable assistance in this area.

[16] Tests on flies trapped in North Carolina are as yet incomplete. Two samples consisting of a total of 428 flies were identified by Dr. M. E. Power, of the Osborn Zoological Laboratory, Yale University, as follows: *Musca domestica*, 349; *Fannia* sp., 26; *Phaenicia sericata*, 22; *Ophyra leucostoma*, 11; *Phormia regina*, 9; *Sarcophaga* sp., 5; *Muscina stabulans*, 2; *Cochliomyia macellaria*, 2; *Lucilia illustris*, 1; and *Bufolucilia silvarum*, 1.

New Haven during this period. These circumstances reduced the possibility of accidental contagion.

The food exposed to flies in North Carolina was fed successfully to chimpanzee "Hickory" (female, aet. 2 years) in approximately one-quart amounts daily for 10 days. The fly-bait was fed in similar quantities for 6 days to chimpanzee "Catawba" (female, aet. 16 months) who relished the bananas but refused the meat and fish. Daily rectal temperatures were taken on both animals (Figs. 1 and 2). Although their temperatures rose to 101° F, neither animal at any time showed evidence of paralytic poliomyelitis. In view of the possibility that either nonparalytic poliomyelitis or an asymptomatic carrier state might be the only form of the experimental disease produced in the test animals, daily specimens of stool from these 2 chimpanzees were collected before and after feeding the test materials. These stools were prepared by ultracentrifugation[17] and tested for virus by intracerebral inoculation in rhesus monkeys.

Results: A record of these tests appears in Table 1 and also in Figures 1 and 2. The control, or pre-feeding, stool specimens of both chimpanzees gave negative tests for poliomyelitis virus, indicating that neither animal was a carrier at the beginning of the experiment. Seven separate stool pools in the post-feeding period have given positive tests for poliomyelitis virus. Thus chimpanzee "Hickory," who ate North Carolina food from July 17 to 27, passed virus in each of 3 stool pools, July 18–29, July 30–Aug. 10, and Aug. 16–24 (Fig. 1). Likewise "Catawba," who received fly-bait from July 17 to 22, had demonstrable virus in 4 stool pools, July 24–Aug. 1, Aug. 11–15, Aug. 25 (single specimen), and Sept. 8–20 (Fig. 2). Typical poliomyelitis lesions were found in the cord and medulla of each of the infected test monkeys.

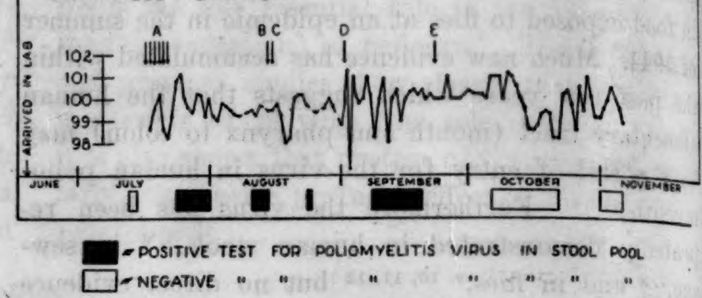

FIG. 2. Detection of poliomyelitis virus in stools of Chimpanzee "Catawba" fed *fly-bait* from North Carolina (A), food from New York (B), fly-bait from Connecticut (C) and from New York (D) and (E).

TABLE 1

RESULTS OF TESTS IN RHESUS MONKEYS FOR VIRUS IN STOOLS OF CHIMPANZEES FED FOOD AND FLY-BAIT

Material fed to chimpanzee				Test for virus in chimpanzee stools				
						Result of inoculation		
						First day of		
Name	Date	Source	Type	Date of stool pools	Rhesus No.	Fever	Paralysis	Lesions
"CATAWBA"	June 19–July 16	Control period		July 13–15	2945	0	0	0
	July 17–22	North Carolina	Fly-bait	July 24—Aug. 1	2894	0	0	0
				" "	2939	14	16	+
				Aug. 11–15	2895	7	11	+
	Aug. 15	New York	Food					
	Aug. 16	Connecticut	Fly-bait	Aug. 25	2896	0	8	+*
	Sept. 2	New York	Fly-bait	Sept. 8–20	2902	0	0†	+
	Sept. 26	New York	Fly-bait	Oct. 6–22	2825	7	0	0
				Nov. 1–7	2897	0	0	0
"HICKORY"	June 19–July 16	Control period			2953	9	0	0
				July 13–15	2961	0	0	0
					2962	0	0	0
	July 17–27	North Carolina	Food					
				July 18–29	2938	4	8	+*
				July 30—Aug. 10	2906	0	0†	+
	Aug. 15	New York	Food					
	Aug. 19	Connecticut	Food and fly-bait	Aug. 16–24	2956	9	21	+
				Sept. 15–21	2807	0	0	0
				Sept. 22–28	2808	13	0	0
				Oct. 11–25	2890	0	0	0
				Nov. 8–15	2957	13	0	0

* Passage of CNS positive in 1 monkey, negative 10 mice, 3 guinea pigs and 3 rabbits.
† Mild weakness of hind legs.

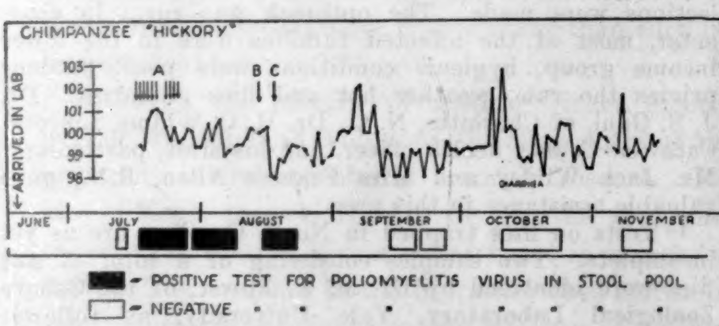

FIG. 1. Detection of poliomyelitis virus in stools of Chimpanzee "Hickory" fed *food* from North Carolina (A), food from New York (B), food and fly-bait from Connecticut (C).

[17] J. L. Melnick, *Jour. Exp. Med.*, 77: 195, 1943.

passage of the strain of virus from two monkeys (representing each chimpanzee, respectively) produced characteristic poliomyelitis in two additional monkeys and was negative in mice, guinea pigs and rabbits. The evidence is clear therefore that poliomyelitis virus appeared in the stools of both chimpanzees in the period immediately after ingestion of food and fly-bait, and also at later periods, 20 days after the last feeding in 1 case, and 3 to 14 days in the other. This suggests the likelihood that the chimpanzees acquired subclinical infections or carrier states and that virus multiplied in them. Although virus was continually eliminated by the chimpanzees for periods of about 1 and 2 months, respectively, it is impossible to state from the present data whether the North Carolina materials were solely responsible or whether materials B, C and D, collected in New York and Connecticut, also contributed.

Discussion: The results of these experiments indicate that food exposed to flies at the homes of poliomyelitis patients in an epidemic area may acquire a quantity of poliomyelitis virus sufficient to produce in chimpanzees by oral administration a non-paralytic infection or asymptomatic carrier state. The question concerning the origin of the virus has three possible answers: the food became contaminated with virus (a) prior to its being exposed at the homes, (b) at the homes by means other than flies or (c) at the homes by flies. With respect to (a), the fact that the bananas were peeled and the skins discarded at the homes makes it unlikely that the bulk of the food was contaminated beforehand, although the sugar and water can not be ruled out. In regard to (b), it is possible that contamination of food occurred by handling or by droplets expelled from an individual's sneezing or coughing, although virus has yet to be demonstrated in human saliva or droplets. On the other hand, the fly-bait, situated beneath a fly-trap which was anchored firmly to the ground, was protected by coarse wire screen and was consequently less accessible to certain other agents such as human beings. The balance of probability would seem to favor fly-contamination at the homes.

The observation that food exposed at infected homes within an epidemic area was found to contain virus, serves as additional evidence to support the following *working hypothesis,* which has been tentatively adopted to guide future investigations along these lines. Human poliomyelitis may be transmitted by a number of different routes. Although the disease may occur at any time of the year the tremendous concentration of cases during the warm season is the result of increased dissemination of virus. This may depend on various factors including something which facilitates the contamination of food by insects such as flies. This is based on the fact that flies have been shown to carry virus and also, as probably indicated in this experiment, to contaminate food.

A further step in the testing of this hypothesis will be to conduct a controlled experimental study on the effect of reducing the number of flies during epidemics of poliomyelitis.

Summary: Poliomyelitis virus has been detected in food exposed to flies at homes of poliomyelitis patients within an epidemic area. This was achieved by feeding such exposed food to chimpanzees which developed subclinical infections or asymptomatic carrier states ascertained by positive stool tests in rhesus monkeys.

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THE EFFECT OF DIETARY PROTEIN INTAKE ON THE XANTHINE OXIDASE ACTIVITY OF RAT LIVER

SARETT *et al.*[1] and Unna *et al.*[2] found that the riboflavin level of rat liver is lowered during low protein ingestion. The latter investigators also showed that the ability of the liver to inactivate estradiol *in vitro* was likewise reduced. We have observed the same phenomena of lowered liver riboflavin level from rats on low protein diet. To study this problem further, we started investigating the effect of dietary protein level on the xanthine oxidase activity of the rat liver when we were forced to discontinue the problem due to the urgency of other work. We believe our results, although very preliminary, are worth reporting.

Rats 10 to 12 weeks old were used. One group was kept on an adequate stock diet, while three other groups were fed diets of the following composition: protein, x per cent.; cerelose, 90-x per cent.; salts, 4 per cent.; hydrogenated cottonseed oil, 4 per cent.; and cellulose (pulverized Cellophane), 2 per cent. A daily supplement of 40 γ each of thiamin, riboflavin and pyridoxine, 100 γ calcium pantothenate, 250 γ nicotinic acid, 6 mg choline and one drop of 1,000A–400D feeding oil was given in supplement cups. All diets were fed *ad libitum.* The total protein content of the four diets was: group 1 (stock), 25 per cent.; group 2, 20 per cent., from casein; group 3, 10 per cent., from soybean oil meal; and group 4, 10 per cent., from corn distillers' solubles.

Xanthine oxidase activity was estimated by the method of Axelrod and Elvehjem[3] adapted to the

[1] H. P. Sarett and W. A. Perlzweig, *Jour. Nutr.*, 25: 173, 1943.

[2] K. Unna, H. O. Singher, C. J. Kensler, H. C. Taylor, Jr., and C. P. Rhoads, *Proc. Soc. Exp. Biol. and Med.*, 55: 254, 1944.

[3] A. E. Axelrod and C. A. Elvehjem, *Jour. Biol. Chem.*, 140: 725, 1941.

Warburg respirometer. All determinations were made in duplicate.

From Table 1 it is seen that the measured xanthine oxidase activity of rat liver is decreased approximately 50 per cent. when the protein in the animals' diet is reduced from 25 per cent. to 20 per cent. When the protein level is lowered to 10 per cent., the measurable xanthine oxidase activity is almost (if not completely) lost.

TABLE 1

EFFECT OF PROTEIN INGESTION ON LIVER XANTHINE OXIDASE ACTIVITY

Group	Number of determinations	Xanthine oxidase activity* Range	Average
Stock—25 per cent. protein	4	1,190–1,690	1,420
20 per cent. casein	4	675–918	745
10 per cent. soybean oil meal	4	0–168†	42
10 per cent. distillers' solubles	5	0–100†	20

* Xanthine oxidase activity is given in cu. mm of oxygen taken up in one hour (during the linear portion of the reaction—endogenous uptake subtracted) per gram of dry weight of tissue.

† In several instances the O_2 uptake for the endogenous sample was slightly greater than for the sample with added xanthine.

We wish to thank Miss M. Mueller for assistance in this study.

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THE INHIBITING EFFECT OF QUINONES ON THE GROWTH OF PENICILLIUM NOTATUM

In the past few years different investigators have studied the inhibitory effect of certain substances on fungi,[1] both saprophytic and pathogenic. Special attention has been given to the inhibitory effect of antibiotic agents, as tyrothricin, pyocyanine and hemipyocyanine on pathogenic fungi.[2] The remarkable antibacterial action of quinones has attracted the attention of various authors.[3,4,5,6] These substances, especially vitamin K, have been suggested as a preventive agency against dental caries,[7, 8, 9] on account of their capacity to prevent the formation of acids in the buccal cavity.

While investigating the metabolism of *Penicillium notatum,* we became interested in studying the effects of certain quinones on the growth of this mold. The following quinones have been used: 2-methyl-1,4-naphthoquinone, hydroquinone and benzoquinone. We also included β-methylnaphthalene in view of its structural similarity to vitamin K.

The substances were added in the desired concentrations to the Czapek-Dox medium which was sterilized by the Seitz filter; the pH was 6.5. The flasks were inoculated with the strain of *P. notatum* 9178 and incubated at 25° C. Results are given in Table 1.

TABLE 1

THE INHIBITING EFFECT OF QUINONES ON THE GROWTH OF PENICILLIUM NOTATUM

	Chemical substances added (mg per 100 ml Czapek-Dox medium)					
	50	25	10	2.5	1.25	0.625
2-Methyl-1,4-naphthoquinone	0	0	0	0	0	1
Hydroquinone	0	0	0	0	1	3
Benzoquinone	0	0	0	1	2	3
β-Methylnaphthalene	2	3	3	3	3	3

0 = no growth; 1 = limited growth; 2 = regular growth; 3 = abundant growth.

In our experiments all the three quinones, even when highly diluted, revealed their capacity of inhibiting the growth of *P. notatum.* The synthetic vitamin K was more active than the other two quinones. Since hydroquinone and benzoquinone have no vitamin activity, our results also suggest that this inhibitory action is a quinone function independent of the capacity to act as vitamin.

β-methylnaphthalene, in spite of being structurally so similar to 2-methyl-1,4-naphthoquinone, had no inhibiting effect on the growth of the mold.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

FILTRATION OF CITRATED PLASMA

It has long been apparent that filtration is the only safe and effective method for the sterilization of citrated plasma. However, all previous work has shown that it is practically impossible to filter large amounts of plasma through the usual bacterial filters.

[1] J. E. Kempf and W. J. Nungester, SCIENCE, 100: 411, 1944.

[2] J. L. Stokes, R. L. Peck and C. R. Woodward, *Proc. Soc. Exp. Biol. and Med.,* 51: 129, 1942.

[3] S. A. Waksman and H. B. Woodruff, *Jour. Bact.,* 44: 373, 1942.

[4] A. E. Oxford and H. Raistrick, *Chem. and Ind.,* 61: 189, 1942.

[5] A. E. Oxford, *Chem. and Ind.,* 61: 128, 1942.

[6] W. D. Armstrong, W. W. Spink and J. Kahnke, *Proc. Soc. Exp. Biol. and Med.,* 52: 136, 1943.

[7] L. S. Fosdick, O. E. Fancher and J. C. Calandra, SCIENCE, 96: 45, 1942.

[8] J. C. Calandra, O. E. Fancher and L. S. Fosdick, *Jour. Dent. Res.,* 23: 31, 1944.

[9] W. D. Armstrong and J. W. Knutson, *Proc. Soc. Exp. Biol. and Med.,* 52: 307, 1943.

n filter candles were employed, it was found that plasma tended to clot during filtration and that pores of these filters quickly became clogged, even gh every effort was made to clarify the plasma re filtration. When the so-called "Seitz" or stos-composition pads were used, a laborious sys- for washing the pads or an arrangement of mul- e pads was necessary to filter relatively small unts of plasma without fear of clotting.

ushby, Buttle and Whitby reported that with a m Seitz filter, an "S. B. Sterilmat" pad and a tive pressure of 20–25 mm mercury, approxi- ely 500 cc of plasma could be filtered without ting.[1] Very soon after this amount had been eded, clots began to appear in the filtrate; and if much as 1,500 cc was filtered, the pad became com- ely blocked with clots. But the amount that ld be filtered might be increased by preliminary ification of the plasma, by wetting the pads be- e they were autoclaved, by washing the pads with ium citrate solution before and between the filtra- of amounts of about 500 cc and by using a com- ation of positive and negative pressures.

Macfarlane, Mainwaring, Macsween and Parish de- bed a method for the filtration of citrated plasma ich required a large number of asbestos pads.[2] ng fourteen 20×20 cm pads, they found that not re than 16 liters of citrated plasma could be filtered lotting was to be prevented. This amount repre- ts only 3 cc of plasma per square centimeter of ring surface.

With a specially prepared asbestos-composition pad ich permits rapid filtration without clotting, we e developed a method for the filtration of plasma a large scale.[3] Using a single 14 cm pad and a ssure of 15–20 pounds, we have been able to filter much as 15–18 liters of plasma without any evi- ce of clotting. A 14 cm pad has an effective er surface of 126.6 square centimeters so that this ount would represent approximately 120 cc–145 cc plasma per square centimeter of filtering surface. cordingly, if six 20×20 cm pads having an effective er surface of 2,103 square centimeters are arranged a filter press, it should be possible to filter at least 9 liters of citrated plasma or 41.5 liters through a gle 20×20 cm pad.

The technique for the filtration of citrated plasma described below was developed primarily for fresh plasma, plasma separated from the red and white cells within 48 hours from the time of bleeding and intended either for freezing or drying.

Blood is received in the standard Red Cross Donor bottles which contain 50 cc of a 4 per cent. solution of sodium citrate for each 500 cc of blood. It is handled in the manner prescribed by the National Institute of Health.[4]

After centrifugation, the plasma is drawn off and pooled. A preservative is added. Then the material is filtered. The final yield of plasma from a bleeding is approximately 300 cc, of which 50 cc is citrate.

A 2,800 cc standard stainless steel Hormann filter, utilizing a 14 cm pad, has been used in this work.[5] However, there is no reason why multiple-plate filters can not be used. A clarifying pad (designated as a K6) and a sterilizing pad (designated as an S6) are placed together in the filter, the K6 pad on top of the S6 pad.[6] The pads need not be washed before they are used. To prevent the asbestos from flaking, a stainless steel screen is placed over the K6 pad. Another stainless steel screen is set on the outlet plate under the S6 pad to insure support. A two-holed size $11\frac{1}{2}$ rubber stopper, one hole for the filter outlet plate and the other for a stainless steel bend to which is attached a bacteria-excluding cotton air filter arrangement, completes the filter unit assembly. The filter unit assembly has been designed to fit into a 20-liter carboy. (See Fig. 1).

The entire filter unit is wrapped and sterilized by autoclaving at 125° C. for one hour. It is advisable to leave the unit loosely assembled during autoclaving in order to avoid distortion of the pads. After autoclaving, the filter and the rubber stopper are introduced under aseptic precautions into a sterile 20-liter carboy. The unit is tightened before the plasma is allowed to flow into the receiving chamber. It should be tightened again soon after the plasma has wetted the pads.

The plasma that is to be filtered is placed in a water bath and warmed to 35°C.–37° C. Warmed to this temperature, plasma under pressure of 15–20 pounds filters rapidly, usually at the rate of 5–7 liters per hour. Vacuum is applied through the air filter arrangement whenever plasma is being introduced into the receiving chamber. After the chamber has been filled, pressure is applied and the vacuum may or may not be continued. Being treated thus, the plasma does

[1] S. R. M. Bushby, G. A. H. Buttle and L. E. H. Whitby, *ncet*, 239: 131–132, 1940.

[2] R. G. Macfarlane, B. R. S. Mainwaring, J. C. Mac- een and H. J. Parish, *Brit. Med. Jour.*, 1: 377–381, 42.

[3] We are indebted to Mr. Warren F. Moore, of Repub- Filters, Paterson, N. J., for his cooperation in the elopment of these pads. In the process of manufac- e the pads are treated in such a manner that they have alcium content of less than 0.01 per cent.

[4] "Minimum Requirements for Unfiltered Normal Human Plasma." 4th revision, May 1, 1944. These minimum requirements must be observed by all processors of normal human plasma for the Military.

[5] Manufactured by the F. R. Hormann Company, Brooklyn, N. Y.

[6] These specially treated pads are available through Mr. Warren F. Moore, Republic Filters, Paterson, N. J.

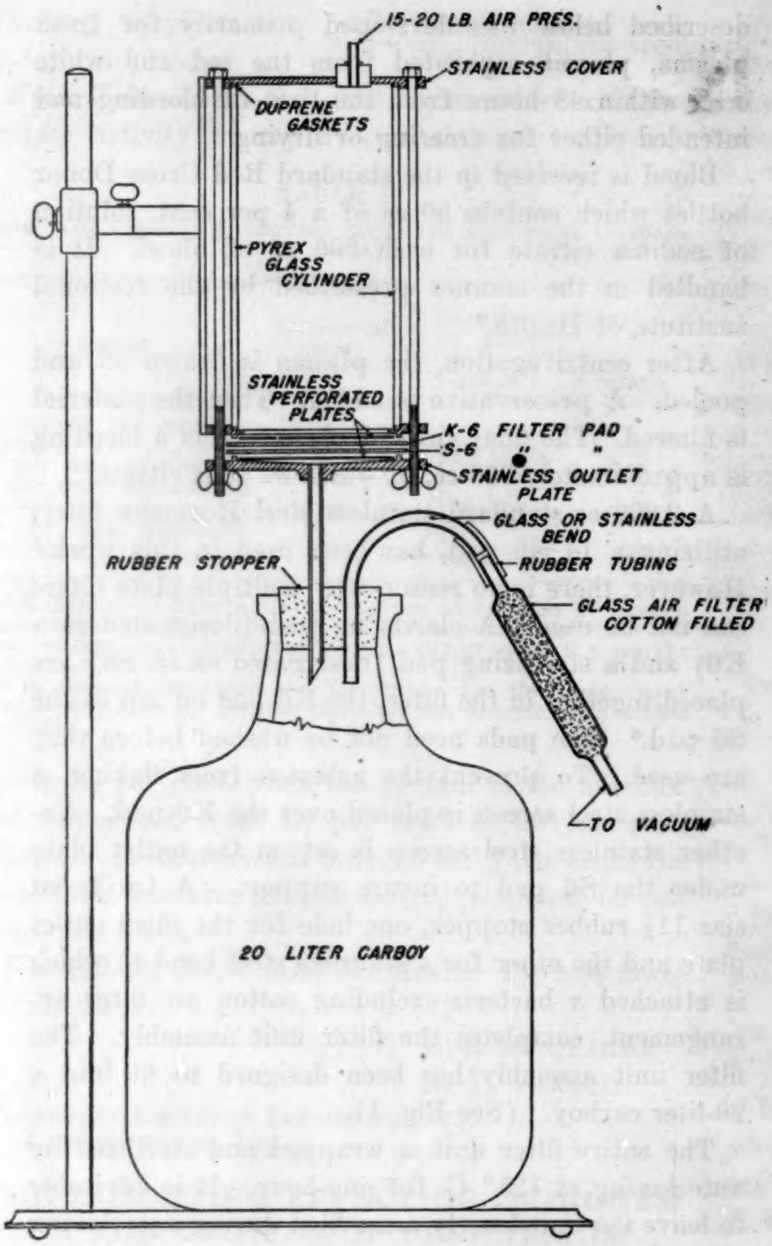

FIG. 1

not remain in contact with the filter pad for any great length of time, an additional precaution to avoid clotting.

When filtration has been completed, the plasma is immediately transferred to final containers and frozen. It has been found desirable that the filling and freezing processes be done within 3–4 hours after filtration.

Over 200 lots, each lot consisting of 15–18 liters of citrated plasma, have been filtered by this method without a single contamination of the final bulk material.

Chemical studies indicate that there is no apparent difference between filtered and unfiltered citrated normal human plasma. These studies will be reported in detail later, but one interesting point may well be mentioned here. It is found that this method of filtration removes traces of red cells so fine that they escape detection by the naked eye.

Summary: Large amounts of fresh citrated plasma can be filtered easily through specially prepared asbestos-composition pads without clotti[ng]. A description of the technique is given.

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EFFICIENT HANDLER FOR SMALL MAMMALS

THE author devised this apparatus shown in Fig which has proved to be extremely useful when rats

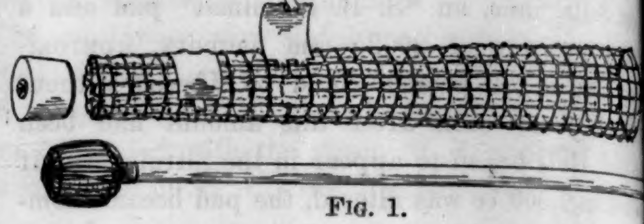

FIG. 1.

wild and hard to manage. It was first used to han large numbers of rats and mice in feeding and oculating experiments without the use of anesthetic The device has been used for a number of years the University of Illinois and is now being used several other universities.

The gadget consists of a wire cloth cone 18 inch long of half-inch mesh for use with rats; a quart inch mesh is better for mice. The large cone he described is 2¾ inches in diameter at one end a tapers to 1¾ inches at the opposite end. Wires clipped out at convenient places near the small e and a sheet metal door with a fastener covers this ope ing. A wooden plunger handle to which is screwed large plunger cork tipped with a sheet metal disk a another large stopper cork with metal disk comple the essential equipment. To insure free movement the cone the plunger cork may be wrapped with wi

To use the instrument insert the stopper cork in t small end of the cone and place the large end into t animal cage so as to crowd the animal into a corne Slip the end of the cone over the head of the rat mouse while holding the cone at about a 45° ang In attempting to escape the animal will run quick up the incline to the stoppered end. The plunger inserted at once and the animal is ready for use. T animal is freed into its cage by pulling the stopp cork and if necessary by stimulating its exit by mea of the plunger.

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